

SEQ 61  
=> s qfghnsvdfeedt/sqep

1 QFGGHNSVDFEEDT/SQEP  
26675 SQL=14  
L13 1 QFGGHNSVDFEEDT/SQEP  
(QFGGHNSVDFEEDT/SQEP AND SQL=14)

=> d sqide

L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS  
RN 142062-19-9 REGISTRY  
CN L-Threonine, L-glutaminy-L-phenylalanylglycylglycyl-L-histidyl-L-  
asparaginy-L-seryl-L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-  
glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*14\*\*\*

SEQ 1 QFGGHNSVDF EEDT  
=====

HITS AT: 1-14  
MF C67 H92 N18 O27  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

3 REFERENCES IN FILE CA (1967 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus uspatfull

=> s 142062-19-9/rn

L14 4 142062-19-9/RN

=> d ibib ab 1-4

L14 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 2000:146776 CAPLUS  
DOCUMENT NUMBER: 132:292413  
TITLE: Synthetic peptide immunogens elicit polyclonal and  
monoclonal antibodies specific for linear epitopes in  
the D motifs of Staphylococcus aureus  
fibronectin-binding protein, which are composed of  
amino acids that are essential for fibronectin binding  
AUTHOR(S): Huesca, Mario; Sun, Qing; Peralta, Robert; Shivji,  
Gulnar M.; Sauder, Daniel N.; McGavin, Martin J.  
CORPORATE SOURCE: Divisions of Microbiology, Laboratory Medicine and  
Pathobiology, Sunnybrook and Women's College Health  
Sciences Centre, North York, ON, M4N 3M5, Can.  
SOURCE: Infect. Immun. (2000), 68(3), 1156-1163  
CODEN: INFIBR; ISSN: 0019-9567  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB A fibronectin (Fn)-binding adhesin of Staphylococcus aureus contains three  
tandem 37- or 38-amino-acid motifs (D1, D2, and D3), which function to  
bind Fn. Plasma from patients with S. aureus infections contain  
antibodies that preferentially recognize ligand induced binding sites in  
the D motifs and do not inhibit Fn binding. To eliminate the influence of

Fn binding on antibody development, the authors used synthetic peptide immunogens D121-34 and D320-33, which each contain a conserved pattern of amino acids that is essential for Fn binding but which cannot bind Fn without N- or C-terminal extensions. The D320-33 immunogen promoted the prodn. of polyclonal antibodies that were 10-fold more effective as inhibitors of Fn-binding to the D3 motif than antibodies obtained by immunizing with an extended peptide D316-36, which exhibits functional Fn binding. The D320-33 immunogen also facilitated the prodn. of a monoclonal antibody, 9C3, which was highly specific for the epitope SVDFEED, and abolished Fn binding by the D3 motif. When mixed with polyclonal anti-D121-34 IgG, 70% inhibition of Fn binding to the three tandem D motifs was achieved compared to no more than 30% inhibition with either antibody prepn. alone. Therefore, by immunizing with short synthetic peptides that are unable to bind Fn, the authors have effectively stimulated the prodn. of antibodies specific for epitopes comprised of amino acids that are essential for Fn binding. Although these epitopes occur within a conserved pattern of amino acids that is required for Fn binding, the antibodies recognized specific linear epitope sequences and not a conserved structure common to all repeated motifs.

REFERENCE COUNT: 40

REFERENCE(S): (3) Balaban, N; Science 1998, V280, P438 CAPLUS  
 (4) Brennan, F; Vaccine 1999, V17, P1846 CAPLUS  
 (5) Casolini, F; Infect Immun 1998, V66, P5433 CAPLUS  
 (6) Fattom, A; Ann Med 1996, V28, P43 CAPLUS  
 (7) Fattom, A; Infect Immun 1996, V64, P1659 CAPLUS  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:509122 CAPLUS

DOCUMENT NUMBER: 129:148069

TITLE: Fibronectin binding protein compositions, antibodies thereto, and methods of use

INVENTOR(S): Hook, Magnus; Patti, Joseph M.; House-Pompeo, Karen L.; Speziale, Petro; Joh, Danny; McGavin, Martin J.

PATENT ASSIGNEE(S): The Texas A & M University System, USA

SOURCE: PCT Int. Appl., 201 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9831389	A2	19980723	WO 1998-US1222	19980121
WO 9831389	A3	19990121		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9866479	A1	19980807	AU 1998-66479	19980121
EP 971740	A2	20000119	EP 1998-908439	19980121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.: US 1997-36139 19970121				
WO 1998-US1222 19980121 .				
AB Disclosed are antibodies that block the binding of fibronectin protein to fibronectin. Also disclosed are site specifically-mutated and truncated				

peptide epitopes derived from the fnbA and fnbB genes of Staphylococcus aureus, the fnbA and fnbB genes of Streptococcus dysgalactiae, and the sfb gene of Streptococcus pyogenes, and nucleic acid segments encoding these peptides and epitopes. The anti-(fibronectin binding site) antibodies, peptides and epitopes that give rise to antibodies that block the binding of fibronectin binding proteins to fibronectin, and DNA segments encoding these proteins and are of use in various screening, diagnostic and therapeutic applications including active and passive immunization and methods for the prevention of streptococcal and staphylococcal colonization in animals or humans. These DNA segments and the peptides derived therefrom are proposed to be of use directly in the prepn. of vaccines and also for use as carrier proteins in vaccine formulations.

L14 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:444088 CAPLUS

DOCUMENT NUMBER: 117:44088

TITLE: Chemically modified fibronectin-binding peptides and fragments

INVENTOR(S): Hoeoek, Magnus; McGavin, Martin; Raucci, Guiseppe

PATENT ASSIGNEE(S): Alfa-Laval Agri International AB, Swed.

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9202555	A1	19920220	WO 1991-SE534	19910809
W: AU, CA, FI, HU, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2067233	AA	19920211	CA 1991-2067233	19910809
AU 9184118	A1	19920302	AU 1991-84118	19910809
AU 632001	B2	19921210		
EP 504335	A1	19920923	EP 1991-914903	19910809
EP 504335	B1	19971210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 61035	A2	19921130	HU 1992-1211	19910809
HU 219261	B	20010328		
JP 05502046	T2	19930415	JP 1991-514015	19910809
AT 161018	E	19971215	AT 1991-914903	19910809
ES 2112862	T3	19980416	ES 1991-914903	19910809
FI 9201582	A	19920409	FI 1992-1582	19920409
NO 9201407	A	19920605	NO 1992-1407	19920409
US 5440014	A	19950808	US 1994-234622	19940428
PRIORITY APPLN. INFO.: SE 1990-2617 A 19900810				
WO 1991-SE534 A 19910809				
US 1992-846995 B1 19920608				
US 1993-55783 B1 19930503				

OTHER SOURCE(S): MARPAT 117:44088

AB Fibronectin-binding peptides R1-PSYQFGGHNSVDFEEDT-R2 (R1 = H, K, DK; R2 = OH, L, LP, LPK) are claimed. Synthetic peptides, peptide fragments, and chem. modified peptides derived from a Staphylococcus aureus fibronectin-binding protein homol. unit (D3) were prepd., and the activity of the peptides (ability to compete with S. aureus cells for binding to 125I-labeled fibronectin or fragment) was detd. The fibronectin-binding region of D3 was reduced to a 14-residue core peptide essential for activity but alone not sufficient to inhibit binding; addn. of a tripeptide to the amino-terminus or carboxy-terminus of this core peptide resulted in a dramatic recovery of activity. The fibronectin-binding peptides of the invention can be used for vaccination, wound healing,

blocking protein receptors, or for an ELISA.

L14 ANSWER 4 OF 4 USPATFULL

ACCESSION NUMBER: 95:71464 USPATFULL

TITLE: Fibronectin binding peptide

INVENTOR(S): Hook, Magnus, 129 Stevens Hill Cir., Birmingham, AL,  
United States 35244  
McGavin, Martin, 1717 Beacon Crest Cir., Birmingham,  
AL, United States 35209  
Raucci, Guiseppe, Via Tito Speri 10, I-00040 Pomezia,  
Rome, Italy

NUMBER KIND DATE

PATENT INFORMATION: US 5440014 19950808

APPLICATION INFO.: US 1994-234622 19940428 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-55783, filed on 3 May  
1993, now abandoned which is a continuation of Ser. No.  
US 1992-846995, filed on 8 Jun 1992, now abandoned

NUMBER DATE

PRIORITY INFORMATION: SE 1990-2617 19900810

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Warden, Jill

ASSISTANT EXAMINER: Marshall, S. G.

LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis

NUMBER OF CLAIMS: 1

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)

LINE COUNT: 679

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A fibronectin binding peptide having the structure R'-PSYQFGGHNS  
VDFEEDT-R.sup.2 wherein R' is hydrogen, K or DK, and R.sup.2 is hydroxy,  
L, LP or LPK is disclosed. The fibronectin binding proteins of the  
present invention may be used, for example, for vaccination of ruminants  
against mastitis caused by Staphylococcal infections, for the treatment  
of wounds, e.g., for blocking protein receptors or for immunization  
(vaccination) against infection by bacterial strains, and for diagnosis  
of bacterial infections caused by Staphylococci strains.

SEQ ID NO: 2

=> s eedtekdkpk/sqep

0 EEDTEKDKPK/SQEP  
72119 SQL=10  
L1 0 EEDTEKDKPK/SQEP  
(EEDTEKDKPK/SQEP AND SQL=10)

=> s eedtekdkpk/sqsp

L2 28 EEDTEKDKPK/SQSP

=> l2 and sql<15

L2 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

For a list of commands available to you in the current file, enter

"HELP COMMANDS" at an arrow prompt (=>).

=> s l2 and sql<15

430200 SQL<15  
L3 1 L2 AND SQL<15

=> d sqide

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 187102-35-8 REGISTRY

CN L-Lysine, L-seryl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.  
.alpha.-aspartyl-L-threonyl-L-.alpha.-glutamyl-L-lysyl-L-.alpha.-aspartyl-  
L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL \*\*\*12\*\*\*

SEQ 1 SFEEDTEKDK PK

=====

HITS AT: 3-12

MF C62 H97 N15 O25

SR CA

LC STN Files: CA, CAPLUS

=> file CAplus

=> s 187102-35-8/rn

1 187102-35-8  
0 187102-35-8D  
L4 1 187102-35-8/RN  
(187102-35-8 (NOTL) 187102-35-8D )

=> d ibib ab

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:97450 CAPLUS

DOCUMENT NUMBER: 126:210757

TITLE: Identification of D motif epitopes in Staphylococcus  
aureus fibronectin-binding protein for the production  
antibody inhibitors of fibronectin binding

AUTHOR(S): Sun, Qing; Smith, Gregory M.; Zahradka, Catherine;

McGavin, Martin J.

CORPORATE SOURCE: Dep. Med. Microbiol., Univ. Manitoba, Winnipeg, MB,  
R3E 0W3, Can.

SOURCE: Infect. Immun. (1997), 65(2), 537-543

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

**AB** A fibronectin-binding protein (FnBP) adhesin of *Staphylococcus aureus* possesses three 37- or 38-amino-acid motifs (D1, D2, and D3) that can each bind fibronectin (Fn) with low affinity and that in tandem comprise D1-3, a high-affinity Fn-binding domain. To identify epitopes for the generation of adhesion-blocking antibodies, rabbits were immunized with recombinant D1-3 or with a glutathione S-transferase fusion protein, GSTD1-3. Affinity-purified antibodies from the D1-3 immunization were poor inhibitors of Fn binding to *S. aureus* and recognized several different epitopes, with a preference for clusters of acidic amino acids that do not contribute to Fn binding. Antibodies generated with GSTD1-3 as an immunogen were more effective inhibitors, but concns. in excess of 20 .mu.g/mL did not promote more than 50% inhibition. These antibodies were highly specific for amino acids 21-34 of D1 (D121-34), which contain a sequence that is essential for Fn binding and are identical to D2 at 12 of 14 residues. Neither antibody prepn. recognized D320-33 of the D3 motif, where the only homol. to D121-34 and D221-34 comprises a sequence motif, GG(X3,4)(I/V)DF, that is crit. to Fn binding. However, antibodies specific for both D121-34 and D320-33 could be obtained by using synthetic peptides corresponding to these sequences as immunogens. F(ab')<sub>2</sub> fragments derived from these antibodies each caused 40-50% inhibition of Fn binding to *S. aureus*, and their ability to bind to purified FnBP was eliminated by competing Fn. However, mixts. of the two F(ab')<sub>2</sub> preps. did not provide additive or synergistic inhibition of Fn binding. Therefore, inhibition of Fn binding to *S. aureus* requires antibodies specific for D121-34 and D320-33, but a mixt. of antibodies specific for both sequences did not provide complete inhibition.

SEQ ID NO: 3

=> s advveyeedtnpgggqvtttesnlvefdeest/sqep

0 ADVVEYEEDTNPGGGQVTTESNLVEFDEEST/SQEP

20879 SQL=31

L5 0 ADVVEYEEDTNPGGGQVTTESNLVEFDEEST/SQEP

(ADVVEYEEDTNPGGGQVTTESNLVEFDEEST/SQEP AND SQL=31)

=> s advveyeedtnpgggqvtttesnlvefdeest/sqsp

L6 6 ADVVEYEEDTNPGGGQVTTESNLVEFDEEST/SQSP

=> s l6 and sql<35

1052946 SQL<35

L7 0 L6 AND SQL<35

=> s l6 and sql<40

1123049 SQL<40

L8 0 L6 AND SQL<40

=> d l6 sqide 1-6

L6 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2001 ACS

RN 364145-35-7 REGISTRY

CN Protein (Staphylococcus aureus clone SAU200916 proliferation-associated  
fragment) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 4247: PN: W00170955 SEQID: 5797 claimed protein

FS PROTEIN SEQUENCE

SQL 1018

SEQ 1 VKNNLRYGIR KHKLGAAASF LGTMIVVGMG QDKEAAASEQ KTTTVEENG

51 SATDNKTSET QTTATNVNHI EETQSYNATV TEQPSNATQV TTEEAPKAVQ

101 APQTAQPANI ETVKEEVVKE EAKPQVKETT QSQDNSGDQR QVDLTPKKAT

151 QNQVAETQVE VAQPRTASES KPRVTRSADV AEAKEASNAK VETGTDVTSK

201 VTVEIGSIEG HNNTNKVEPH AGQRAVLKYK LKFENGLHQG DYFDFTLSNN

251 VNTHGVSTAR KVPEIKNGSV VMATGEVLEG GKIRYTFTND IEDKVDVTAE

301 LEINLFIDPK TVQTNGNQTI TSTLNEEQTS KELDVKYKDG IGNYYANLNG

351 SIETFNKANN RFSHVAFIKP NNGKTTSVTV TGTLMKGSNQ NGNQPKVRIF

401 EYLGNNEDIA KSVYANTTDT SKFKEVTSNM SGNLNLQNNG SYSLNIENLD

451 KTYVVHYDGE YLNGTDEVDF RTQMVGHPAQ LYKYYYDRGY TLTWDNGLVL

501 YSNKANGNGK NGPIIQNNKF EYKEDTIKET LTGQYDKNLV TTVEEYDSS

551 TLDIDYHTAI DGGGGYVDGY IETIEETDSS AIDIDYHTAV DSEAGHVGGY

601 TESSEESNPI DFEESTHENS KHHADVVEYE EDTNPGGGQV TTESNLVEFD

=====

651 EESTKGIVTG AVSDHTTVED TKEYTTESNL IELVDELPEE HGQAQGPVEE

=====

701 ITENNHSH SGLGTENGHG NYDVIEEIEE NSHVDIKSEL GYEGGQNSGN

751 QSFEEDTEED KPKYEQGGNI VDIDFDSVPQ IHGQNKGNQS FEEDTEKDKP

801 KYEHGGNIID IDFDSVPHIH GFNKHTEIIE EDTNKDKPSY QFGGHNSVDF

851 EEDTLPKVSG QNEGQQTIEE DTPPIVPPT PPTPEVPSEP ETPTPTPEV

901 PSEPETPTPP TPEVPSEPET PTPPTPEVPA EPGKPVPPAK EEPKKPSKPV

951 EQGKVVTPVI EINEKVKAVA PTKKPQSKKS ELPETGGEES TNKGMLFGGL

1001 FSILGLALLR RNKKNHKA

HITS AT: 624-654

MF Unspecified

CI MAN

SR CA

LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L6 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2001 ACS  
RN 341089-10-9 REGISTRY  
CN Fibronectin-binding protein (Staphylococcus aureus strain Mu50 gene fnb)  
(9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN GenBank AP003365-derived protein GI 14248277  
FS PROTEIN SEQUENCE  
SQL 1038

SEQ 1 MKNNLRYGIR KHKLGAAVSF LGTMIVVGMG QDKEAAASEQ KTTTVEENG  
51 SATDNKTSET QTTATNVNHI EETQSYNATV TEQPSNATQV TTEEAPKAVQ  
101 APQTAQPANV ETVKEEEKPQ VKETTQPQDN SGNQRQVDLT PKKVTQNQGT  
151 ETQVEVAQPR TASESKPRVT RSADVAEAKE ASDVSEVKGT DVTSKVTVES  
201 GSIEAPQGNK VEPHAGQRVV LKYKLFADG LKRGDYDFDT LSNNVNTYGV  
251 STARKVPEIK NGSVVMATGE ILGNNGNIRYT FTNEIEHKVE VTANLEINLF  
301 IDPKTVQSNG EQKITSKLNQ EETEKTIPTVV YNPGVSNSYT NVNGSIETFN  
351 KESNKFTHIA YIKPMNGNQS NTVSVTGTLT EGSNLAGGQP TVKVVEYLK  
401 KDELPSQSVYA NTSNTNKFVD VTKEMNGKLS VQDNGSYSLN LDKLDKTYVI  
451 HYTG EYLQGS DQVNFRT ELY GYPERAYKSY YVYGGYRLTW DNGLVLYSNK  
501 ADGNGKNGQI IQDNDFEYKE DTAKGTMSGQ YDAKQIETE ENQDNTPLDI  
551 DYHTAIDGEG GYVDGYIETI EETDSSAIDI DYHTAVDSEV GHVGGYTES  
601 EESNPIDFEE STHENSKHHA DVVEYEEDTN PGGGQVTTES NLVEFDEEST  
=====

651 KGIVTGAVSD HTTIEDTKEY TTESNLIELV DELPEEHGQA QGP IEEITEN  
701 NHHISHSLG TENGHGNYGV IEEIEENSHV DIKSELGYEG QONSGNQSF  
751 EDTEEDKPKY EQGGNIVDID FDSVPQIHGQ NKGDQSFEED TEKDKPKYEH  
801 GGNIIDIDFD SVPQIHGFNK HNEIEEDTN KDKPNYQFGG HNSVDFEEDT  
851 LPKVSGQNEG QQTIEEDTTP PTPPTPEVPS EPETPMPTPT EVPTSEPPT  
901 PTPPEVPSEP ETPTPTPEV PSEPPTPTTP TPEVPSEPET PTPPTPEVPA  
951 EPGKPVPPAK EEPKKPSKPV EQGKVVTPI EINEKVKAVA PTKKAQSKKS  
1001 ELPETGGEES TNKGMLFGGL FSILGLALLR RNKKNNKA

HITS AT: 620-650  
MF Unspecified  
CI MAN  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER  
1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L6 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2001 ACS  
RN 341089-09-6 REGISTRY  
CN Fibronectin-binding protein (Staphylococcus aureus strain Mu50 gene fnbB)  
(9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN GenBank AP003365-derived protein GI 14248276  
FS PROTEIN SEQUENCE  
SQL 961

SEQ 1 MKNLRYGIR KHKLGAAVSF LGTMIVVGMG QEKEAAASEQ NNTTVEESGS  
51 SATESKASET QTTNNVNTI DETQSYSATS TEQPSKSTQV TTEEAPTTVQ  
101 APKVETEMKS QEDLPSEKVA DKETTGTQVD IAQPSNVSEI KPRMKRSADV  
151 TAVSEKEVAE EAKATGTDVT NKVEVTESSL EGHNKDSNIV NPHNAQRVTL  
201 KYKWKFGEGI KAGDYDFDTL SDNVETHGIS TLRKVPEIKS STEDKVMANG  
251 QVINERTIRY TFTDYINNKK DLTAELNLLN FIDPTTVTKQ GSQKVEVTLG  
301 QNKVSKEFDI KYLDGVKDRM GVTVNGRIDT LNKEEGKFSH FAYVKPNNQS  
351 LTSVTVTGQV TSGYKQSANN PTVKVYKHIG SDELAESVYA KLDDTSKFED  
401 VTEKVNLSYT SNGGYTLNLG DLDNSKDYVI KYEGEYDQNA KDLNFRTHLS  
451 GYHKYYPYYP YYPYYPVQLT WNGVAFYSN NAKGDGKDKP NDPIIEKSEP  
501 IDLDIKSEPP VEKHELTGTI EESNDSKPID FEYHTAVEGA EGHAEGIIET



551 EEDSIHVDFE ESTHENS KHH ADVVEYEEDT NPGGGQVTTE SNLVEFDEES

=====

601 TKGIVTGA VS DHTTVEDTKE YTTESNLI ELVDELPEEHGQ AQGP IEEITE

=

651 NNHHISHSGL GTENGHGNYG VIDEIEENSH VDIKSELGYE GGQNSGNQSF  
701 EEDTEEDKPK YEQGGNIVDI DFDSVPQIHG QNNGNQSFEE DTEEDKPKYE  
751 QGGNIIDIDF DSVQIHGFN KHNEIIEEDT NKDKPNYQFG GHNSVDFEED  
801 TLPKVSGQNE GQQTIEEDTT PPTPPTPEVP SEPETPTPTPT PEVPSEPGEP  
851 TPPKPEVPSE PETPVPPTPE VPSEPGKVP PAKKEPKKPS KPVEQGKVVT  
901 PVIEINEKVK AVAPTKQKQS KKS ELPETGG EESTNKGMLF GGLFSILGLV  
951 LLRRNKKNNK A

HITS AT: 571-601

MF Unspecified

CI MAN

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L6 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2001 ACS

RN 195127-37-8 REGISTRY

CN Protein (Staphylococcus aureus fibronectin/fibrinogen-binding open reading  
frame 54\_6) (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL 1027

SEQ 1 ILHLKGDIIV KNNLRYGIRK HKLGAASVFL GTMIVVGMGQ DKEAAASEQK  
51 TTTVEENGNS ATDNKTSETQ TTATNVN HIE ETQSYNATVT EQPSNATQVT  
101 TEEAPKAVQA PQTAQPANIE TVKEEVVKEE AKPQVKETTQ SQDNSGDQRQ  
151 VDLTPKKATQ NQVAETQVEV AQPRTASESK PRVTRSADVA EAKEASNAKV  
201 ETGTDVTSKV TVEIGSIEGH NNTNKVEPHA GQRAVLKYKL KFENGLHQGD  
251 YFDFTLNNV NTHGVSTARK VPEIKNGSVV MATGEVLEGG KIRYTFNDI  
301 EDKVDVTAEL EINLFIDPKT VQTNGNQTTIT STLNEEQTSK ELDVKYKDGI  
351 GNYYANLNGS IETFNKANNR FSHVAFIKPN NGKTTSVTVT GTLMKGSNQN  
401 GNQPKVRIFE YLGNNEDIAK SVYANTTDTS KFKEVTSNMS GNLNLQNNGS  
451 YSLNIENLDK TYVVHYDGEY LNGTDEVDFR TQMVGHPEQL YKYYYDRGYT  
501 LTWDNGLVLY SNKANGNEKN GPIQNNKFE YKEDTIKETL TGQYDKNLVT  
551 TVEEYDSST LDIDYHTAID GGGGYVDGYI ETIEETDSSA IDIDYHTAVD  
601 SEAGHVGGYT ESSEESNPID FEESTHENS KHHADVVEYEE DTNPGGGQVT

=====

651 TESNLVEFDE ESTKGIVTGA VSDHTTVEDT KEYTTESNLI ELVDELPEEH

=====

701 GQAQGPVEEI TKNNHHISHS GLGTENGHGN YDVIEEIEEN SHVDIKSEKG  
751 YEGGQNSGNQ SFEEDTEEDK PKYEQGGNIV DIDFDSVPQI HGQNKGNQSF  
801 EEDTEKDKPK YEHGGNIIDI DFDSVPHIHG FNKHTEIEE DTNKDKPSYQ  
851 FGGHNSVDFE EDTLPKVSGQ NEGQQTIEED TTPPIVPPTPTPTPEVPSEPE  
901 TPTPPTPEVP SEPETPTPTPT PEVPSEPETP TPPTPEVPAE PGKVPVPAKE  
951 EPKKPSKPVE QGKVVTPIE INEKVKAVAP TKKPQSKKSE LPETGGEEST  
1001 NKGMLFGGLF SILGLALLRR NKNHKA

HITS AT: 633-663

MF Unspecified

CI MAN

SR CA

LC STN Files: CA, CAPLUS, TOXLIT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L6 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2001 ACS

RN 122784-68-3 REGISTRY

CN Protein FnBP (Staphylococcus aureus clone pFR001 precursor) (9CI) (CA  
INDEX NAME)

FS PROTEIN SEQUENCE

SQL 1018

SEQ 1 VKNNLRYGIR KHKLGAASVF LGTMIVVGMG QDKEAAASEQ KTTTVEENG  
51 SATDNKTSET QTTATNVNHI EETRSYNATV TEQPSNATQV TTEEAPKAVQ  
101 APQTAQPANI ETVKEEVVKE EAKPRVKETT QSQDNSGDQR QVDLTPKKAT  
151 QNQVAETQVE VAQPRTASES KPRVTRSADV AEAKEASNAK VETGTDVTSK  
201 VTVEIGSIEG HNNTNKVEPH AGQRAVLKYK LKFENGLHQG DYFDFTLSNN  
251 VNTHGVSTAR KVPEIKNGSV VMATGEVLEG GKIRYTFTND IQDKVDVTAE  
301 LEINLFIDPK TVQTNGNQTI TSTLNEEQTS KELDVKYKDG IGNYANLNG  
351 SIETFNKANN RFSHVAFIKP NNGKTTSTVT TGTLMKGSNQ NGNQPKVRIF  
401 EYLGNNEDIA KSVYANTTDT SKFKEVTSNM SGNLNLQNNG SYSLNIENLD  
451 KTYVVHYDGE YLNGTDEVDF RTQMVGHPEQ LYKYYYDRGY TLTDWNGLV  
501 YSNKANGNEK NGPIIQNNKF EYKEDTIKET LTGQYDKNLV TTVEEYDSS  
551 TLDIDYHTAI DGGGGYVDGY IETIEETDSS AIDIDYHTAV DSEAGHVG  
601 TESSEESNPI DFEESTHENS KHHADVVEYE EDTNPGGGQV TTESNLVEFD

=====

651 EESTKGIVTG AVSDHTTVED TKEYTTESNL IELVDELPEE HGQAQGPVEE

=====

701 ITKNNHHISH SGLGTENGHG NYDVIEEIEE NSHVDIKSEL GYEGGQNSGN  
751 QSFEEDTEED KPKYEQGGNI VDIDFDSVPQ IHGQNKGNQS FEEDTEKDKP  
801 KYEHGGNIID IDFDSVPHIH GFNKHTEIIE EDTNKDKPSY QFGGHNSVDF  
851 EEDTLPKVSG QNEGQQTIEE DTPPIVPPT PPTPEVPSEP EPTPTPEV  
901 PSEPPTPTP TPEVPSEPET PTPPTPEVPA EPGKVPVPAK EEPKKPSKPV  
951 EQGKVVTPIV EINEKVKAVA PTKKPQSKKS ELPETGGEES TNKGMLFGGL  
1001 FSILGLALLR RNKKNHKA

HITS AT: 624-654

MF Unspecified

CI MAN

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L6 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2001 ACS

RN 122784-67-2 REGISTRY

CN Protein FnBP (Staphylococcus aureus clone pFR001) (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL 982

SEQ 1 ASEQKTTTVE ENGNSATDNK TSETQTTATN VNHIETRSY NATVTEQPSN  
51 ATQVTTEEAP KAVQAPQTAQ PANIETVKEE VVKEEAKPRV KETTQSQDNS  
101 GDQRQVDLTP KKATQNQVAE TQVEVAQPRT ASES KPRVTR SADVAEAKA  
151 SNAK VETGTD VTSKVTVEIG SIEGHNNTNK VEPHAGQRAV LKYKLKFENG  
201 LHQGDYFDFT LSNNVNTHGV STARKVPEIK NGSVVMATGE VLEGGKIRYT  
251 FTNDIQDKVD VTAELEINLF IDPKTVQTNG NQTITSTLNE EQTSKELDVK  
301 YKDGIGNYYA NLNGSIETFN KANNRFSHVA FIKPNNGKTT SVTVTGTLMK  
351 GSNQNGNQPK VRIFEYLGNN EDIAKSVYAN TTDTSKFKEV TSNMSGNLNL  
401 QNNGSYSLNI ENLDKTYVVH YDGEYLNGLD EVDFTQMVG HPEQLYKYYY  
451 DRGYTLTDWN GLVLYSNKAN GNEKNGPIIQ NNFYEYKEDT IKETLTGQYD  
501 KNLVTTVEEE YDSSTLDIDY HTAIDGGGGY VDGYYETIEE TDSSAIDIDY  
551 HTAVDSEAGH VGGYTESSEE SNPIDFEEST HENSKHHADV VEYEEDTNPG

====

601 GGQVTTESNL VEFDEESTKG IVTGAVSDHT TVEDTKEYTT ESNLIELVDE

=====

651 LPEEHGQAQG PVEEITKNNH HISHSGLGTE NGHGNVDVIE EIEENSHVDI  
701 KSELGYEGGQ NSGNQSFEED TEEDKPKYEQ GGNIVDIDFD SVPQIHGQNK  
751 GNQSFEEDTE KDKPKYEHGG NIIDIDFDSV PHIHGFNKHT EIEEDTNKD  
801 KPSYQFGGHN SVDFEEDTLP KVSGQNEGQQ TIEEDTTPPI VPPTPTPEV  
851 PSEPPTPTP TPEVPSEPET PTPPTPEVPS EPETPTPTP EVPAEPGKPV  
901 PPAKEPKPK SKPVEQKVV TPVIEINEKV KAVAPTKKPQ SKKSELPETG  
951 GEESTNKGML FGGLFSILGL ALLRRNKKNH KA

HITS AT: 588-618

MF Unspecified

CI MAN

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL  
2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

SEQ ID NO: 5

=> s qnsgnqsfeedteedkpkyeqggnivdidfdsvpqihg/sqep

1 QNSGNQSFEEDTEEDKPKYEQGGNIVDIDFDSVPQIHG/SQEP

23669 SQL=38

L9 1 QNSGNQSFEEDTEEDKPKYEQGGNIVDIDFDSVPQIHG/SQEP

(QNSGNQSFEEDTEEDKPKYEQGGNIVDIDFDSVPQIHG/SQEP AND SQL=38)

=> d sqide

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 119977-17-2 REGISTRY

CN Glycine, L-glutaminy-L-asparaginy-L-serylglycyl-L-asparaginy-L-glutaminy-L-seryl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-threonyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-lysyl-L-prolyl-L-lysyl-L-tyrosyl-L-.alpha.-glutamyl-L-glutaminyglycylglycyl-L-asparaginy-L-isoleucyl-L-valyl-L-.alpha.-aspartyl-L-isoleucyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-seryl-L-valyl-L-prolyl-L-glutaminy-L-isoleucyl-L-histidyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL \*\*\*38\*\*\*

SEQ 1 QNSGNQSFEEDTEEDKPKYE QGGNIVDIDFDSVPQIHG

HITS AT: 1-38

MF C181 H269 N49 O71

CI MAN

SR CA

LC STN Files: CA, CAPLUS, TOXLIT

3 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus toxlit

=> s 119977-17-2/rn

'RN' IS NOT A VALID FIELD CODE

L10 3 119977-17-2/RN

=> d ibib ab 1-3

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:97450 CAPLUS

DOCUMENT NUMBER: 126:210757

TITLE: Identification of D motif epitopes in Staphylococcus aureus fibronectin-binding protein for the production antibody inhibitors of fibronectin binding

AUTHOR(S): Sun, Qing; Smith, Gregory M.; Zahradka, Catherine; McGavin, Martin J.

CORPORATE SOURCE: Dep. Med. Microbiol., Univ. Manitoba, Winnipeg, MB, R3E 0W3, Can.

SOURCE: Infect. Immun. (1997), 65(2), 537-543

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A fibronectin-binding protein (FnBP) adhesin of Staphylococcus aureus possesses three 37- or 38-amino-acid motifs (D1, D2, and D3) that can each

bind fibronectin (Fn) with low affinity and that in tandem comprise D1-3, a high-affinity Fn-binding domain. To identify epitopes for the generation of adhesion-blocking antibodies, rabbits were immunized with recombinant D1-3 or with a glutathione S-transferase fusion protein, GSTD1-3. Affinity-purified antibodies from the D1-3 immunization were poor inhibitors of Fn binding to *S. aureus* and recognized several different epitopes, with a preference for clusters of acidic amino acids that do not contribute to Fn binding. Antibodies generated with GSTD1-3 as an immunogen were more effective inhibitors, but concns. in excess of 20  $\mu\text{g/mL}$  did not promote more than 50% inhibition. These antibodies were highly specific for amino acids 21-34 of D1 (D121-34), which contain a sequence that is essential for Fn binding and are identical to D2 at 12 of 14 residues. Neither antibody prep. recognized D320-33 of the D3 motif, where the only homol. to D121-34 and D221-34 comprises a sequence motif, GG(X3,4)(I/V)DF, that is crit. to Fn binding. However, antibodies specific for both D121-34 and D320-33 could be obtained by using synthetic peptides corresponding to these sequences as immunogens.  $\text{F(ab')}_2$  fragments derived from these antibodies each caused 40-50% inhibition of Fn binding to *S. aureus*, and their ability to bind to purified FnBP was eliminated by competing Fn. However, mixts. of the two  $\text{F(ab')}_2$  preps. did not provide additive or synergistic inhibition of Fn binding. Therefore, inhibition of Fn binding to *S. aureus* requires antibodies specific for D121-34 and D320-33, but a mixt. of antibodies specific for both sequences did not provide complete inhibition.

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:452661 CAPLUS

DOCUMENT NUMBER: 121:52661

TITLE: Interaction of N-terminal fragments of fibronectin with synthetic and recombinant D motifs from its binding protein on *Staphylococcus aureus* studied using fluorescence anisotropy

AUTHOR(S): Huff, Sheela; Matsuka, Yury V.; McGavin, Martin J.; Ingham, Kenneth C.

CORPORATE SOURCE: Holland Lab., Am. Red. Cross, Rockville, MD, 20855, USA

SOURCE: J. Biol. Chem. (1994), 269(22), 15563-70

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The N-terminal 29-kDa fragment of fibronectin (Fn29K) contains five type I "finger" modules. It binds to heparin, fibrin, and bacteria and is involved in fibronectin (Fn) matrix assembly. Binding to *Staphylococcus aureus* involves a cell wall-assocd. protein that contains approx. three repeats of a 38-residue D motif (Signas, C., Raucci, G., Jonsson, K., Lindgren, P.-E., Anantharamaiah, G. M., Hook, M., and Lindberg, M. (1989) Proc. Natl. Acad. Sci. U.S.A. 86, 699-703). Synthetic peptides representing D1, D2, and D3, when labeled with fluorescein isothiocyanate (FITC), exhibited increases in fluorescence anisotropy upon addn. of Fn29K but not other Fn fragments. The response could be reversed by titrn. with unlabeled peptides to yield inhibition consts. that agreed with the dissocn. consts. obtained by fitting the initial response. Values of  $K_d$  ranged between 2 and 12  $\mu\text{M}$ , with D3 having the highest affinity. Specificity of D3 for Fn29K was further illustrated by the fact that its C-terminal half (D3b, Lys801 to Lys821), when immobilized, selectively adsorbed Fn29K from a thermolysin digest of fibronectin. The binding site in Fn was further localized within Fn29K by analyzing smaller proteolytic or recombinant subfragments. Those contg. fingers, F3-5 and F4-5, were purified on D3b-Sepharose and bound FITC-D3b with  $K_d$  values of 4-6  $\mu\text{M}$ . Subfragments contg. pairs of fingers 1-2, 2-3, or single fingers 1, 4, or 5 were inactive. Whole D1-3, expressed in *Escherichia coli* and labeled with fluorescein, bound 1.9 mol/mol of Fn29K with  $K_d = 1.5 \text{ nM}$ . F4-5 and

F2-3 bound with resp. K<sub>d</sub> values of 0.35 and 4.4  $\mu$ M. These and other results indicate that binding of the individual D region peptides is mediated through their C-terminal halves, primarily to fingers 4 and 5 of fibronectin. The possible basis of the much higher affinity of D1-3 is discussed.

L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1989:609813 CAPLUS

DOCUMENT NUMBER: 111:209813

TITLE: Nucleotide sequence of the gene for a  
fibronectin-binding protein from *Staphylococcus*  
*aureus*: use of this peptide sequence in the synthesis  
of biologically active peptides

AUTHOR(S): Signaes, Christer; Raucci, Giuseppe; Joensson, Klas;  
Lindgren, Per Eric; Anantharamaiah, G. M.; Hoeoek,  
Magnus; Lindberg, Martin

CORPORATE SOURCE: Dep. Microbiol., Swed. Univ. Agric. Sci., Uppsala,  
S-750 07, Swed.

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1989), 86(2), 699-703  
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Binding of cells of *S. aureus* to fibronectin, which may present a mechanism of host tissue adherence, involves a fibronectin-receptor protein present on the bacterial surface. Cloning of a gene coding for a staphylococcal fibronectin-binding protein and construction of a fusion protein with fibronectin-binding properties were previously reported. The gene sequence and the deduced primary sequence of the fibronectin-binding protein were subsequently detd. The protein resembles other cell-wall-assocd. proteins on Gram-pos. bacteria in that it (i) appears to be anchored in the cell membrane via its C-terminal end, (ii) contains a proline-rich repeating unit outside the membrane anchor, and (iii) contains a long (36-amino acid) signal sequence at the N-terminus. The fibronectin-binding activity has been localized to a domain composed of a 38-amino acid unit repeated completely 3 times and partially a fourth time; the identity between the three 38-amino acid sequences varies from 42 to 87%. Three synthetic peptides mimicking the structure of each 38-amino acid unit were constructed. All 3 peptides interacted with fibronectin, as indicated by their ability to inhibit binding of fibronectin to staphylococcal cells, whereas an unrelated 37-amino acid peptide showed no inhibitory activity.

SEQ 7

=> s qnkgnsfeedtekdkpkkyehggniididfdsvphihg/sqep

1 QNKGNSFEEDTEKDKPKYEHGGNIIDIDFDSVPHIHG/SQEP

23669 SQL=38

L13 1 QNKGNSFEEDTEKDKPKYEHGGNIIDIDFDSVPHIHG/SQEP

(QNKGNSFEEDTEKDKPKYEHGGNIIDIDFDSVPHIHG/SQEP AND SQL=38)

=> d sqide

L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 119977-19-4 REGISTRY

CN Glycine, L-glutaminy-L-asparaginy-L-lysylglycyl-L-asparaginy-L-glutaminy-L-seryl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-threonyl-L-.alpha.-glutamyl-L-lysyl-L-.alpha.-aspartyl-L-lysyl-L-prolyl-L-lysyl-L-tyrosyl-L-.alpha.-glutamyl-L-histidylglycylglycyl-L-asparaginy-L-isoleucyl-L-isoleucyl-L-.alpha.-aspartyl-L-isoleucyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-seryl-L-valyl-L-prolyl-L-histidyl-L-isoleucyl-L-histidyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL \*\*\*38\*\*\*

SEQ 1 QNKGNSFEE DTEKDKPKYE HGGNIIDIDF DSVPHIHG

=====

HITS AT: 1-38

MF C188 H281 N53 O66

CI MAN

SR CA

LC STN Files: CA, CAPLUS, TOXLIT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus

=> s 119977-19-4/rn

2 119977-19-4

0 119977-19-4D

L14 2 119977-19-4/RN

(119977-19-4 (NOTL) 119977-19-4D )

=> d ibib ab 1 2

L14 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:97450 CAPLUS

DOCUMENT NUMBER: 126:210757

TITLE: Identification of D motif epitopes in Staphylococcus aureus fibronectin-binding protein for the production antibody inhibitors of fibronectin binding

AUTHOR(S): Sun, Qing; Smith, Gregory M.; Zahradka, Catherine; McGavin, Martin J.

CORPORATE SOURCE: Dep. Med. Microbiol., Univ. Manitoba, Winnipeg, MB, R3E 0W3, Can.

SOURCE: Infect. Immun. (1997), 65(2), 537-543

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A fibronectin-binding protein (FnBP) adhesin of *Staphylococcus aureus* possesses three 37- or 38-amino-acid motifs (D1, D2, and D3) that can each bind fibronectin (Fn) with low affinity and that in tandem comprise D1-3, a high-affinity Fn-binding domain. To identify epitopes for the generation of adhesion-blocking antibodies, rabbits were immunized with recombinant D1-3 or with a glutathione S-transferase fusion protein, GSTD1-3. Affinity-purified antibodies from the D1-3 immunization were poor inhibitors of Fn binding to *S. aureus* and recognized several different epitopes, with a preference for clusters of acidic amino acids that do not contribute to Fn binding. Antibodies generated with GSTD1-3 as an immunogen were more effective inhibitors, but concns. in excess of 20 .mu.g/mL did not promote more than 50% inhibition. These antibodies were highly specific for amino acids 21-34 of D1 (D121-34), which contain a sequence that is essential for Fn binding and are identical to D2 at 12 of 14 residues. Neither antibody prepn. recognized D320-33 of the D3 motif, where the only homol. to D121-34 and D221-34 comprises a sequence motif, GG(X3,4)(I/V)DF, that is crit. to Fn binding. However, antibodies specific for both D121-34 and D320-33 could be obtained by using synthetic peptides corresponding to these sequences as immunogens. F(ab')<sub>2</sub> fragments derived from these antibodies each caused 40-50% inhibition of Fn binding to *S. aureus*, and their ability to bind to purified FnBP was eliminated by competing Fn. However, mixts. of the two F(ab')<sub>2</sub> prepn. did not provide additive or synergistic inhibition of Fn binding. Therefore, inhibition of Fn binding to *S. aureus* requires antibodies specific for D121-34 and D320-33, but a mixt. of antibodies specific for both sequences did not provide complete inhibition.

L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1989:609813 CAPLUS

DOCUMENT NUMBER: 111:209813

TITLE: Nucleotide sequence of the gene for a  
fibronectin-binding protein from *Staphylococcus*  
*aureus*: use of this peptide sequence in the synthesis  
of biologically active peptides

AUTHOR(S): Signaes, Christer; Raucci, Giuseppe; Joensson, Klas;  
Lindgren, Per Eric; Anantharamaiah, G. M.; Hoeoek,  
Magnus; Lindberg, Martin

CORPORATE SOURCE: Dep. Microbiol., Swed. Univ. Agric. Sci., Uppsala,  
S-750 07, Swed.

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1989), 86(2), 699-703  
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Binding of cells of *S. aureus* to fibronectin, which may present a mechanism of host tissue adherence, involves a fibronectin-receptor protein present on the bacterial surface. Cloning of a gene coding for a staphylococcal fibronectin-binding protein and construction of a fusion protein with fibronectin-binding properties were previously reported. The gene sequence and the deduced primary sequence of the fibronectin-binding protein were subsequently detd. The protein resembles other cell-wall-assocd. proteins on Gram-pos. bacteria in that it (i) appears to be anchored in the cell membrane via its C-terminal end, (ii) contains a proline-rich repeating unit outside the membrane anchor, and (iii) contains a long (36-amino acid) signal sequence at the N-terminus. The fibronectin-binding activity has been localized to a domain composed of a 38-amino acid unit repeated completely 3 times and partially a fourth time; the identity between the three 38-amino acid sequences varies from 42 to 87%. Three synthetic peptides mimicking the structure of each 38-amino acid unit were constructed. All 3 peptides interacted with fibronectin, as indicated by their ability to inhibit binding of fibronectin to staphylococcal cells, whereas an unrelated 37-amino acid peptide showed no inhibitory activity.



SEQ ID NO: 9

=> s kpsyqfghnsvdfeedtlpk/sqep

1 KPSYQFGGHNSVDFEEDTLPK/SQEP

50328 SQL=21

L17 1 KPSYQFGGHNSVDFEEDTLPK/SQEP

(KPSYQFGGHNSVDFEEDTLPK/SQEP AND SQL=21)

=> d sqide

L17 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 142062-16-6 REGISTRY

CN L-Lysine, L-lysyl-L-prolyl-L-seryl-L-tyrosyl-L-glutamyl-L-phenylalanyl-glycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-threonyl-L-leucyl-L-prolyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL \*\*\*21\*\*\*

SEQ 1 KPSYQFGGHNSVDFEEDTLP K

=====

HITS AT: 1-21

MF C107 H155 N27 O36

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

=> file caplus

=> s 142062-16-6/rn

3 142062-16-6

0 142062-16-6D

L18 3 142062-16-6/RN

(142062-16-6 (NOTL) 142062-16-6D )

=> d ibib ab 1-3

L18 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:146776 CAPLUS

DOCUMENT NUMBER: 132:292413

TITLE: Synthetic peptide immunogens elicit polyclonal and monoclonal antibodies specific for linear epitopes in the D motifs of Staphylococcus aureus fibronectin-binding protein, which are composed of amino acids that are essential for fibronectin binding

AUTHOR(S): Huesca, Mario; Sun, Qing; Peralta, Robert; Shivji, Gulnar M.; Sauder, Daniel N.; McGavin, Martin J.

CORPORATE SOURCE: Divisions of Microbiology, Laboratory Medicine and Pathobiology, Sunnybrook and Women's College Health Sciences Centre, North York, ON, M4N 3M5, Can.

SOURCE: Infect. Immun. (2000), 68(3), 1156-1163

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A fibronectin (Fn)-binding adhesin of Staphylococcus aureus contains three tandem 37- or 38-amino-acid motifs (D1, D2, and D3), which function to bind Fn. Plasma from patients with S. aureus infections contain antibodies that preferentially recognize ligand induced binding sites in the D motifs and do not inhibit Fn binding. To eliminate the influence of

Fn binding on antibody development, the authors used synthetic peptide immunogens D121-34 and D320-33, which each contain a conserved pattern of amino acids that is essential for Fn binding but which cannot bind Fn without N- or C-terminal extensions. The D320-33 immunogen promoted the prodn. of polyclonal antibodies that were 10-fold more effective as inhibitors of Fn-binding to the D3 motif than antibodies obtained by immunizing with an extended peptide D316-36, which exhibits functional Fn binding. The D320-33 immunogen also facilitated the prodn. of a monoclonal antibody, 9C3, which was highly specific for the epitope SVDFEED, and abolished Fn binding by the D3 motif. When mixed with polyclonal anti-D121-34 IgG, 70% inhibition of Fn binding to the three tandem D motifs was achieved compared to no more than 30% inhibition with either antibody prepn. alone. Therefore, by immunizing with short synthetic peptides that are unable to bind Fn, the authors have effectively stimulated the prodn. of antibodies specific for epitopes comprised of amino acids that are essential for Fn binding. Although these epitopes occur within a conserved pattern of amino acids that is required for Fn binding, the antibodies recognized specific linear epitope sequences and not a conserved structure common to all repeated motifs.

REFERENCE COUNT: 40

REFERENCE(S): (3) Balaban, N; Science 1998, V280, P438 CAPLUS  
 (4) Brennan, F; Vaccine 1999, V17, P1846 CAPLUS  
 (5) Casolini, F; Infect Immun 1998, V66, P5433 CAPLUS  
 (6) Fattom, A; Ann Med 1996, V28, P43 CAPLUS  
 (7) Fattom, A; Infect Immun 1996, V64, P1659 CAPLUS  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:452661 CAPLUS

DOCUMENT NUMBER: 121:52661

TITLE: Interaction of N-terminal fragments of fibronectin  
 with synthetic and recombinant D motifs from its  
 binding protein on Staphylococcus aureus studied using  
 fluorescence anisotropy

AUTHOR(S): Huff, Sheela; Matsuka, Yury V.; McGavin, Martin J.;  
 Ingham, Kenneth C.

CORPORATE SOURCE: Holland Lab., Am. Red. Cross, Rockville, MD, 20855,  
 USA

SOURCE: J. Biol. Chem. (1994), 269(22), 15563-70  
 CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The N-terminal 29-kDa fragment of fibronectin (Fn29K) contains five type I "finger" modules. It binds to heparin, fibrin, and bacteria and is involved in fibronectin (Fn) matrix assembly. Binding to Staphylococcus aureus involves a cell wall-assocd. protein that contains .apprx.three repeats of a 38-residue D motif (Signas, C., Raucci, G., Jonsson, K., Lindgren, P.-E., Anantharamaiah, G. M., Hook, M., and Lindberg, M. (1989) Proc. Natl. Acad. Sci. U.S.A. 86, 699-703). Synthetic peptides representing D1, D2, and D3, when labeled with fluorescein isothiocyanate (FITC), exhibited increases in fluorescence anisotropy upon addn. of Fn29K but not other Fn fragments. The response could be reversed by titrn. with unlabeled peptides to yield inhibition constns. that agreed with the dissocn. constns. obtained by fitting the initial response. Values of Kd ranged between 2 and 12 .mu.M, with D3 having the highest affinity. Specificity of D3 for Fn29K was further illustrated by the fact that its C-terminal half (D3b, Lys801 to Lys821), when immobilized, selectively adsorbed Fn29K from a thermolysin digest of fibronectin. The binding site in Fn was further localized within Fn29K by analyzing smaller proteolytic or recombinant subfragments. Those contg. fingers, F3-5 and F4-5, were purified on D3b-Sepharose and bound FITC-D3b with Kd values of 4-6 .mu.m. Subfragments contg. pairs of fingers 1-2, 2-3, or single fingers 1, 4, or

5 were inactive. Whole D1-3, expressed in Escherichia coli and labeled with fluorescein, bound 1.9 mol/mol of Fn29K with Kd = 1.5 nM. F4-5 and F2-3 bound with resp. Kd values of 0.35 and 4.4 .mu.M. These and other results indicate that binding of the individual D region peptides is mediated through their C-terminal halves, primarily to fingers 4 and 5 of fibronectin. The possible basis of the much higher affinity of D1-3 is discussed.

L18 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:444088 CAPLUS

DOCUMENT NUMBER: 117:44088

TITLE: Chemically modified fibronectin-binding peptides and fragments

INVENTOR(S): Hoeoek, Magnus; McGavin, Martin; Raucci, Guiseppe

PATENT ASSIGNEE(S): Alfa-Laval Agri International AB, Swed.

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9202555	A1	19920220	WO 1991-SE534	19910809
W: AU, CA, FI, HU, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2067233	AA	19920211	CA 1991-2067233	19910809
AU 9184118	A1	19920302	AU 1991-84118	19910809
AU 632001	B2	19921210		
EP 504335	A1	19920923	EP 1991-914903	19910809
EP 504335	B1	19971210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 61035	A2	19921130	HU 1992-1211	19910809
HU 219261	B	20010328		
JP 05502046	T2	19930415	JP 1991-514015	19910809
AT 161018	E	19971215	AT 1991-914903	19910809
ES 2112862	T3	19980416	ES 1991-914903	19910809
FI 9201582	A	19920409	FI 1992-1582	19920409
NO 9201407	A	19920605	NO 1992-1407	19920409
US 5440014	A	19950808	US 1994-234622	19940428
PRIORITY APPLN. INFO.: SE 1990-2617 A 19900810				
WO 1991-SE534 A 19910809				
US 1992-846995 B1 19920608				
US 1993-55783 B1 19930503				

OTHER SOURCE(S): MARPAT 117:44088

AB Fibronectin-binding peptides R1-PSYQFGGHNSVDFEEDT-R2 (R1 = H, K, DK; R2 = OH, L, LP, LPK) are claimed. Synthetic peptides, peptide fragments, and chem. modified peptides derived from a Staphylococcus aureus fibronectin-binding protein homol. unit (D3) were prepd., and the activity of the peptides (ability to compete with S. aureus cells for binding to 125I-labeled fibronectin or fragment) was detd. The fibronectin-binding region of D3 was reduced to a 14-residue core peptide essential for activity but alone not sufficient to inhibit binding; addn. of a tripeptide to the amino-terminus or carboxy-terminus of this core peptide resulted in a dramatic recovery of activity. The fibronectin-binding peptides of the invention can be used for vaccination, wound healing,

L19 ANSWER 1 OF 1 USPATFULL

ACCESSION NUMBER: 95:71464 USPATFULL

TITLE: Fibronectin binding peptide

INVENTOR(S): Hook, Magnus, 129 Stevens Hill Cir., Birmingham, AL,  
United States 35244  
McGavin, Martin, 1717 Beacon Crest Cir., Birmingham,  
AL, United States 35209  
Raucci, Guiseppe, Via Tito Speri 10, I-00040 Pomezia,  
Rome, Italy

NUMBER KIND DATE  
-----

PATENT INFORMATION: US 5440014 19950808  
APPLICATION INFO.: US 1994-234622 19940428 (8)  
RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-55783, filed on 3 May  
1993, now abandoned which is a continuation of Ser. No.  
US 1992-846995, filed on 8 Jun 1992, now abandoned

NUMBER DATE  
-----

PRIORITY INFORMATION: SE 1990-2617 19900810  
DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Warden, Jill  
ASSISTANT EXAMINER: Marshall, S. G.  
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis  
NUMBER OF CLAIMS: 1  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)  
LINE COUNT: 679

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A fibronectin binding peptide having the structure R'-PSYQFGGHNS  
VDFEEDT-R.sup.2 wherein R' is hydrogen, K or DK, and R.sup.2 is hydroxy,  
L, LP or LPK is disclosed. The fibronectin binding proteins of the  
present invention may be used, for example, for vaccination of ruminants  
against mastitis caused by Staphylococcal infections, for the treatment  
of wounds, e.g., for blocking protein receptors or for immunization  
(vaccination) against infection by bacterial strains, and for diagnosis  
of bacterial infections caused by Staphylococci strains.

SEQ 60  
=> s qggnivdidfdsvp/sqep

1 QGGNIVDIDFDSVP/SQEP  
26675 SQL=14  
L11 1 QGGNIVDIDFDSVP/SQEP  
(QGGNIVDIDFDSVP/SQEP AND SQL=14)

=> d sqide

L11 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS  
RN 187102-34-7 REGISTRY  
CN L-Proline, L-glutaminylglycylglycyl-L-asparaginyL-L-isoleucyl-L-valyl-L-  
.alpha.-aspartyl-L-isoleucyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-  
aspartyl-L-seryl-L-valyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*14\*\*\*

SEQ 1 QGGNIVDIDF DSV  
=====

HITS AT: 1-14  
MF C64 H98 N16 O24  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus

=> s 187102-34-7/rn

2 187102-34-7  
0 187102-34-7D  
L12 2 187102-34-7/RN  
(187102-34-7 (NOTL) 187102-34-7D )

=> d ibib ab 1 2

L12 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 1998:509122 CAPLUS  
DOCUMENT NUMBER: 129:148069  
TITLE: Fibronectin binding protein compositions, antibodies  
thereto, and methods of use  
INVENTOR(S): Hook, Magnus; Patti, Joseph M.; House-Pompeo, Karen  
L.; Speziale, Petro; Joh, Danny; McGavin, Martin J.  
PATENT ASSIGNEE(S): The Texas A & M University System, USA  
SOURCE: PCT Int. Appl., 201 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9831389	A2	19980723	WO 1998-US1222	19980121
WO 9831389	A3	19990121		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,  
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,  
FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,  
GA, GN, ML, MR, NE, SN, TD, TG

AU 9866479 A1 19980807 AU 1998-66479 19980121

EP 971740 A2 20000119 EP 1998-908439 19980121

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1997-36139 19970121

WO 1998-US1222 19980121

**AB** Disclosed are antibodies that block the binding of fibronectin protein to fibronectin. Also disclosed are site specifically-mutated and truncated peptide epitopes derived from the *fnbA* and *fnbB* genes of *Staphylococcus aureus*, the *fnbA* and *fnbB* genes of *Streptococcus dysgalactiae*, and the *sfb* gene of *Streptococcus pyogenes*, and nucleic acid segments encoding these peptides and epitopes. The anti-(fibronectin binding site) antibodies, peptides and epitopes that give rise to antibodies that block the binding of fibronectin binding proteins to fibronectin, and DNA segments encoding these proteins and are of use in various screening, diagnostic and therapeutic applications including active and passive immunization and methods for the prevention of streptococcal and staphylococcal colonization in animals or humans. These DNA segments and the peptides derived therefrom are proposed to be of use directly in the prepn. of vaccines and also for use as carrier proteins in vaccine formulations.

L12 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:97450 CAPLUS

DOCUMENT NUMBER: 126:210757

**TITLE:** Identification of D motif epitopes in *Staphylococcus aureus* fibronectin-binding protein for the production antibody inhibitors of fibronectin binding

**AUTHOR(S):** Sun, Qing; Smith, Gregory M.; Zahradka, Catherine; McGavin, Martin J.

**CORPORATE SOURCE:** Dep. Med. Microbiol., Univ. Manitoba, Winnipeg, MB, R3E 0W3, Can.

**SOURCE:** Infect. Immun. (1997), 65(2), 537-543  
CODEN: INFIBR; ISSN: 0019-9567

**PUBLISHER:** American Society for Microbiology

**DOCUMENT TYPE:** Journal

**LANGUAGE:** English

**AB** A fibronectin-binding protein (FnBP) adhesin of *Staphylococcus aureus* possesses three 37- or 38-amino-acid motifs (D1, D2, and D3) that can each bind fibronectin (Fn) with low affinity and that in tandem comprise D1-3, a high-affinity Fn-binding domain. To identify epitopes for the generation of adhesion-blocking antibodies, rabbits were immunized with recombinant D1-3 or with a glutathione S-transferase fusion protein, GSTD1-3. Affinity-purified antibodies from the D1-3 immunization were poor inhibitors of Fn binding to *S. aureus* and recognized several different epitopes, with a preference for clusters of acidic amino acids that do not contribute to Fn binding. Antibodies generated with GSTD1-3 as an immunogen were more effective inhibitors, but concns. in excess of 20 .mu.g/mL did not promote more than 50% inhibition. These antibodies were highly specific for amino acids 21-34 of D1 (D121-34), which contain a sequence that is essential for Fn binding and are identical to D2 at 12 of 14 residues. Neither antibody prepn. recognized D320-33 of the D3 motif, where the only homol. to D121-34 and D221-34 comprises a sequence motif, GG(X3,4)(I/V)DF, that is crit. to Fn binding. However, antibodies specific for both D121-34 and D320-33 could be obtained by using synthetic peptides corresponding to these sequences as immunogens. F(ab')<sub>2</sub>

fragments derived from these antibodies each caused 40-50% inhibition of Fn binding to *S. aureus*, and their ability to bind to purified FnBP was eliminated by competing Fn. However, mixts. of the two F(ab')<sub>2</sub> preps. did not provide additive or synergistic inhibition of Fn binding. Therefore, inhibition of Fn binding to *S. aureus* requires antibodies specific for D121-34 and D320-33, but a mixt. of antibodies specific for both sequences did not provide complete inhibition.

SEQ 86

=> s vdfeedtlpkv/sqep

1 VDFEEDTLPKV/SQEP

28732 SQL=11

L18 1 VDFEEDTLPKV/SQEP

(VDFEEDTLPKV/SQEP AND SQL=11)

=> d sqide

L18 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 187102-36-9 REGISTRY

CN L-Valine, L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-threonyl-L-leucyl-L-prolyl-L-lysyl-(9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL \*\*\*11\*\*\*

SEQ 1 VDFEEDTLPK V

=====

HITS AT: 1-11

MF C58 H90 N12 O21

SR CA

LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus

=> s 187102-36-9/rn

1 187102-36-9

0 187102-36-9D

L19 1 187102-36-9/RN

(187102-36-9 (NOTL) 187102-36-9D )

=> d ibib ab

L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:97450 CAPLUS

DOCUMENT NUMBER: 126:210757

TITLE: Identification of D motif epitopes in Staphylococcus aureus fibronectin-binding protein for the production antibody inhibitors of fibronectin binding

AUTHOR(S): Sun, Qing; Smith, Gregory M.; Zahradka, Catherine; McGavin, Martin J.

CORPORATE SOURCE: Dep. Med. Microbiol., Univ. Manitoba, Winnipeg, MB, R3E 0W3, Can.

SOURCE: Infect. Immun. (1997), 65(2), 537-543

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A fibronectin-binding protein (FnBP) adhesin of Staphylococcus aureus possesses three 37- or 38-amino-acid motifs (D1, D2, and D3) that can each bind fibronectin (Fn) with low affinity and that in tandem comprise D1-3, a high-affinity Fn-binding domain. To identify epitopes for the generation of adhesion-blocking antibodies, rabbits were immunized with



recombinant D1-3 or with a glutathione S-transferase fusion protein, GSTD1-3. Affinity-purified antibodies from the D1-3 immunization were poor inhibitors of Fn binding to *S. aureus* and recognized several different epitopes, with a preference for clusters of acidic amino acids that do not contribute to Fn binding. Antibodies generated with GSTD1-3 as an immunogen were more effective inhibitors, but concns. in excess of 20  $\mu\text{g/mL}$  did not promote more than 50% inhibition. These antibodies were highly specific for amino acids 21-34 of D1 (D121-34), which contain a sequence that is essential for Fn binding and are identical to D2 at 12 of 14 residues. Neither antibody prep. recognized D320-33 of the D3 motif, where the only homol. to D121-34 and D221-34 comprises a sequence motif, GG(X<sub>3</sub>,4)(I/V)DF, that is crit. to Fn binding. However, antibodies specific for both D121-34 and D320-33 could be obtained by using synthetic peptides corresponding to these sequences as immunogens. F(ab')<sub>2</sub> fragments derived from these antibodies each caused 40-50% inhibition of Fn binding to *S. aureus*, and their ability to bind to purified FnBP was eliminated by competing Fn. However, mixts. of the two F(ab')<sub>2</sub> preps. did not provide additive or synergistic inhibition of Fn binding. Therefore, inhibition of Fn binding to *S. aureus* requires antibodies specific for D121-34 and D320-33, but a mixt. of antibodies specific for both sequences did not provide complete inhibition.

SEQ 87  
ONLY 5 AMINO ACIDS!!!!!!!!!!!!!! enablement as to functional language????  
=> s feedt/sqep

0 FEEDT/SQEP  
44972 SQL=5  
L22 0 FEEDT/SQEP  
(FEEDT/SQEP AND SQL=5)

=> s feedt/sqsp

L23 142 FEEDT/SQSP

=> s l23 and sql<10

252831 SQL<10  
L24 0 L23 AND SQL<10

=> s l23 and sql<15

430429 SQL<15  
L26 5 L23 AND SQL<15

=> d sqide 1-5

L26 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2001 ACS  
RN 264234-56-2 REGISTRY  
CN L-Leucine, L-phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-  
valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-  
glutamyl-L-.alpha.-aspartyl-L-threonyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*14\*\*\*

SEQ 1 FGGHNSVDFE EDTL  
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HITS AT: 9-13  
MF C68 H95 N17 O26  
SR CA  
LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L26 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2001 ACS  
RN 187102-36-9 REGISTRY  
CN L-Valine, L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-  
.alpha.-glutamyl-L-.alpha.-aspartyl-L-threonyl-L-leucyl-L-prolyl-L-lysyl-  
(9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*11\*\*\*

SEQ 1 VDFEEDTLPK V  
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HITS AT: 3-7  
MF C58 H90 N12 O21  
SR CA  
LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L26 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2001 ACS  
RN 187102-35-8 REGISTRY  
CN L-Lysine, L-seryl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-threonyl-L-.alpha.-glutamyl-L-lysyl-L-.alpha.-aspartyl-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*12\*\*\*

SEQ 1 SFEEDTEKDK PK

=====

HITS AT: 2-6  
MF C62 H97 N15 O25  
SR CA  
LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L26 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2001 ACS  
RN 187102-33-6 REGISTRY  
CN L-Glutamic acid, L-seryl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-threonyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-lysyl-L-prolyl-L-lysyl-L-tyrosyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*14\*\*\*

SEQ 1 SFEEDTEEDK PKYE

=====

HITS AT: 2-6  
MF C75 H108 N16 O32  
SR CA  
LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L26 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2001 ACS  
RN 142062-19-9 REGISTRY  
CN L-Threonine, L-glutamyl-L-phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*14\*\*\*

SEQ 1 QFGGHNSVDF EEDT

= =====

HITS AT: 10-14  
MF C67 H92 N18 O27  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

3 REFERENCES IN FILE CA (1967 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus

=> s 264234-56-2/rn

1 264234-56-2  
0 264234-56-2D

L27 1 264234-56-2/RN  
(264234-56-2 (NOTL) 264234-56-2D )

=> d ibib ab

L27 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:146776 CAPLUS

DOCUMENT NUMBER: 132:292413

TITLE: Synthetic peptide immunogens elicit polyclonal and monoclonal antibodies specific for linear epitopes in the D motifs of Staphylococcus aureus fibronectin-binding protein, which are composed of amino acids that are essential for fibronectin binding

AUTHOR(S): Huesca, Mario; Sun, Qing; Peralta, Robert; Shivji, Gulnar M.; Sauder, Daniel N.; McGavin, Martin J.

CORPORATE SOURCE: Divisions of Microbiology, Laboratory Medicine and Pathobiology, Sunnybrook and Women's College Health Sciences Centre, North York, ON, M4N 3M5, Can.

SOURCE: Infect. Immun. (2000), 68(3), 1156-1163

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A fibronectin (Fn)-binding adhesin of Staphylococcus aureus contains three tandem 37- or 38-amino-acid motifs (D1, D2, and D3), which function to bind Fn. Plasma from patients with S. aureus infections contain antibodies that preferentially recognize ligand induced binding sites in the D motifs and do not inhibit Fn binding. To eliminate the influence of Fn binding on antibody development, the authors used synthetic peptide immunogens D121-34 and D320-33, which each contain a conserved pattern of amino acids that is essential for Fn binding but which cannot bind Fn without N- or C-terminal extensions. The D320-33 immunogen promoted the prodn. of polyclonal antibodies that were 10-fold more effective as inhibitors of Fn-binding to the D3 motif than antibodies obtained by immunizing with an extended peptide D316-36, which exhibits functional Fn binding. The D320-33 immunogen also facilitated the prodn. of a monoclonal antibody, 9C3, which was highly specific for the epitope SVDFEED, and abolished Fn binding by the D3 motif. When mixed with polyclonal anti-D121-34 IgG, 70% inhibition of Fn binding to the three tandem D motifs was achieved compared to no more than 30% inhibition with either antibody prepn. alone. Therefore, by immunizing with short synthetic peptides that are unable to bind Fn, the authors have effectively stimulated the prodn. of antibodies specific for epitopes comprised of amino acids that are essential for Fn binding. Although these epitopes occur within a conserved pattern of amino acids that is required for Fn binding, the antibodies recognized specific linear epitope sequences and not a conserved structure common to all repeated motifs.

REFERENCE COUNT: 40

REFERENCE(S): (3) Balaban, N; Science 1998, V280, P438 CAPLUS

(4) Brennan, F; Vaccine 1999, V17, P1846 CAPLUS

(5) Casolini, F; Infect Immun 1998, V66, P5433 CAPLUS

(6) Fattom, A; Ann Med 1996, V28, P43 CAPLUS

(7) Fattom, A; Infect Immun 1996, V64, P1659 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 187102-36-9/rn

1 187102-36-9

0 187102-36-9D

L28 1 187102-36-9/RN

(187102-36-9 (NOTL) 187102-36-9D )

=> d ibib ab

L28 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:97450 CAPLUS

DOCUMENT NUMBER: 126:210757

TITLE: Identification of D motif epitopes in *Staphylococcus aureus* fibronectin-binding protein for the production of antibody inhibitors of fibronectin binding

AUTHOR(S): Sun, Qing; Smith, Gregory M.; Zahradka, Catherine; McGavin, Martin J.

CORPORATE SOURCE: Dep. Med. Microbiol., Univ. Manitoba, Winnipeg, MB, R3E 0W3, Can.

SOURCE: Infect. Immun. (1997), 65(2), 537-543  
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A fibronectin-binding protein (FnBP) adhesin of *Staphylococcus aureus* possesses three 37- or 38-amino-acid motifs (D1, D2, and D3) that can each bind fibronectin (Fn) with low affinity and that in tandem comprise D1-3, a high-affinity Fn-binding domain. To identify epitopes for the generation of adhesion-blocking antibodies, rabbits were immunized with recombinant D1-3 or with a glutathione S-transferase fusion protein, GSTD1-3. Affinity-purified antibodies from the D1-3 immunization were poor inhibitors of Fn binding to *S. aureus* and recognized several different epitopes, with a preference for clusters of acidic amino acids that do not contribute to Fn binding. Antibodies generated with GSTD1-3 as an immunogen were more effective inhibitors, but concns. in excess of 20 .mu.g/mL did not promote more than 50% inhibition. These antibodies were highly specific for amino acids 21-34 of D1 (D121-34), which contain a sequence that is essential for Fn binding and are identical to D2 at 12 of 14 residues. Neither antibody prepn. recognized D320-33 of the D3 motif, where the only homol. to D121-34 and D221-34 comprises a sequence motif, GG(X3,4)(I/V)DF, that is crit. to Fn binding. However, antibodies specific for both D121-34 and D320-33 could be obtained by using synthetic peptides corresponding to these sequences as immunogens. F(ab')<sub>2</sub> fragments derived from these antibodies each caused 40-50% inhibition of Fn binding to *S. aureus*, and their ability to bind to purified FnBP was eliminated by competing Fn. However, mixts. of the two F(ab')<sub>2</sub> preps. did not provide additive or synergistic inhibition of Fn binding. Therefore, inhibition of Fn binding to *S. aureus* requires antibodies specific for D121-34 and D320-33, but a mixt. of antibodies specific for both sequences did not provide complete inhibition.

=> s 187102-35-8/rn

1 187102-35-8

0 187102-35-8D

L29 1 187102-35-8/RN

(187102-35-8 (NOTL) 187102-35-8D )

=> d ibib ab

L29 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:97450 CAPLUS

DOCUMENT NUMBER: 126:210757

TITLE: Identification of D motif epitopes in *Staphylococcus*

aureus fibronectin-binding protein for the production  
antibody inhibitors of fibronectin binding  
AUTHOR(S): Sun, Qing; Smith, Gregory M.; Zahradka, Catherine;  
McGavin, Martin J.  
CORPORATE SOURCE: Dep. Med. Microbiol., Univ. Manitoba, Winnipeg, MB,  
R3E 0W3, Can.  
SOURCE: Infect. Immun. (1997), 65(2), 537-543  
CODEN: INFIBR; ISSN: 0019-9567  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

=> s 187102-33-6/rn

1 187102-33-6  
0 187102-33-6D  
L30 1 187102-33-6/RN  
(187102-33-6 (NOTL) 187102-33-6D )

=> d ibib ab

L30 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 1997:97450 CAPLUS  
DOCUMENT NUMBER: 126:210757  
TITLE: Identification of D motif epitopes in Staphylococcus  
aureus fibronectin-binding protein for the production  
antibody inhibitors of fibronectin binding  
AUTHOR(S): Sun, Qing; Smith, Gregory M.; Zahradka, Catherine;  
McGavin, Martin J.  
CORPORATE SOURCE: Dep. Med. Microbiol., Univ. Manitoba, Winnipeg, MB,  
R3E 0W3, Can.  
SOURCE: Infect. Immun. (1997), 65(2), 537-543  
CODEN: INFIBR; ISSN: 0019-9567  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

=> s 142062-19-9/rn

3 142062-19-9  
0 142062-19-9D  
L31 3 142062-19-9/RN  
(142062-19-9 (NOTL) 142062-19-9D )

=> d ibib ab 1-3

L31 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 2000:146776 CAPLUS  
DOCUMENT NUMBER: 132:292413  
TITLE: Synthetic peptide immunogens elicit polyclonal and  
monoclonal antibodies specific for linear epitopes in  
the D motifs of Staphylococcus aureus  
fibronectin-binding protein, which are composed of  
amino acids that are essential for fibronectin binding  
AUTHOR(S): Huesca, Mario; Sun, Qing; Peralta, Robert; Shivji,  
Gulnar M.; Sauder, Daniel N.; McGavin, Martin J.  
CORPORATE SOURCE: Divisions of Microbiology, Laboratory Medicine and  
Pathobiology, Sunnybrook and Women's College Health  
Sciences Centre, North York, ON, M4N 3M5, Can.

SOURCE: Infect. Immun. (2000), 68(3), 1156-1163

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A fibronectin (Fn)-binding adhesin of *Staphylococcus aureus* contains three tandem 37- or 38-amino-acid motifs (D1, D2, and D3), which function to bind Fn. Plasma from patients with *S. aureus* infections contain antibodies that preferentially recognize ligand induced binding sites in the D motifs and do not inhibit Fn binding. To eliminate the influence of Fn binding on antibody development, the authors used synthetic peptide immunogens D121-34 and D320-33, which each contain a conserved pattern of amino acids that is essential for Fn binding but which cannot bind Fn without N- or C-terminal extensions. The D320-33 immunogen promoted the prodn. of polyclonal antibodies that were 10-fold more effective as inhibitors of Fn-binding to the D3 motif than antibodies obtained by immunizing with an extended peptide D316-36, which exhibits functional Fn binding. The D320-33 immunogen also facilitated the prodn. of a monoclonal antibody, 9C3, which was highly specific for the epitope SVDFEED, and abolished Fn binding by the D3 motif. When mixed with polyclonal anti-D121-34 IgG, 70% inhibition of Fn binding to the three tandem D motifs was achieved compared to no more than 30% inhibition with either antibody prepn. alone. Therefore, by immunizing with short synthetic peptides that are unable to bind Fn, the authors have effectively stimulated the prodn. of antibodies specific for epitopes comprised of amino acids that are essential for Fn binding. Although these epitopes occur within a conserved pattern of amino acids that is required for Fn binding, the antibodies recognized specific linear epitope sequences and not a conserved structure common to all repeated motifs.

REFERENCE COUNT: 40

REFERENCE(S): (3) Balaban, N; Science 1998, V280, P438 CAPLUS

(4) Brennan, F; Vaccine 1999, V17, P1846 CAPLUS

(5) Casolini, F; Infect Immun 1998, V66, P5433 CAPLUS

(6) Fattom, A; Ann Med 1996, V28, P43 CAPLUS

(7) Fattom, A; Infect Immun 1996, V64, P1659 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:509122 CAPLUS

DOCUMENT NUMBER: 129:148069

TITLE: Fibronectin binding protein compositions, antibodies thereto, and methods of use

INVENTOR(S): Hook, Magnus; Patti, Joseph M.; House-Pompeo, Karen L.; Speziale, Petro; Joh, Danny; McGavin, Martin J.

PATENT ASSIGNEE(S): The Texas A & M University System, USA

SOURCE: PCT Int. Appl., 201 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9831389	A2	19980723	WO 1998-US1222	19980121
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WO 9831389	A3	19990121		
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W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,

FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,  
GA, GN, ML, MR, NE, SN, TD, TG  
AU 9866479 A1 19980807 AU 1998-66479 19980121  
EP 971740 A2 20000119 EP 1998-908439 19980121  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO  
PRIORITY APPLN. INFO.: US 1997-36139 19970121  
WO 1998-US1222 19980121

AB Disclosed are antibodies that block the binding of fibronectin protein to fibronectin. Also disclosed are site specifically-mutated and truncated peptide epitopes derived from the fnbA and fnbB genes of Staphylococcus aureus, the fnbA and fnbB genes of Streptococcus dysgalactiae, and the sfb gene of Streptococcus pyogenes, and nucleic acid segments encoding these peptides and epitopes. The anti-(fibronectin binding site) antibodies, peptides and epitopes that give rise to antibodies that block the binding of fibronectin binding proteins to fibronectin, and DNA segments encoding these proteins and are of use in various screening, diagnostic and therapeutic applications including active and passive immunization and methods for the prevention of streptococcal and staphylococcal colonization in animals or humans. These DNA segments and the peptides derived therefrom are proposed to be of use directly in the prepn. of vaccines and also for use as carrier proteins in vaccine formulations.

L31 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:444088 CAPLUS

DOCUMENT NUMBER: 117:44088

TITLE: Chemically modified fibronectin-binding peptides and fragments

INVENTOR(S): Hooeek, Magnus; McGavin, Martin; Raucci, Guiseppe

PATENT ASSIGNEE(S): Alfa-Laval Agri International AB, Swed.

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9202555	A1	19920220	WO 1991-SE534	19910809
W: AU, CA, FI, HU, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2067233	AA	19920211	CA 1991-2067233	19910809
AU 9184118	A1	19920302	AU 1991-84118	19910809
AU 632001	B2	19921210		
EP 504335	A1	19920923	EP 1991-914903	19910809
EP 504335	B1	19971210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 61035	A2	19921130	HU 1992-1211	19910809
HU 219261	B	20010328		
JP 05502046	T2	19930415	JP 1991-514015	19910809
AT 161018	E	19971215	AT 1991-914903	19910809
ES 2112862	T3	19980416	ES 1991-914903	19910809
FI 9201582	A	19920409	FI 1992-1582	19920409
NO 9201407	A	19920605	NO 1992-1407	19920409
US 5440014	A	19950808	US 1994-234622	19940428
PRIORITY APPLN. INFO.: SE 1990-2617 A 19900810				
WO 1991-SE534 A 19910809				
US 1992-846995 B1 19920608				
US 1993-55783 B1 19930503				

OTHER SOURCE(S): MARPAT 117:44088

AB Fibronectin-binding peptides R1-PSYQFGGHNSVDFEEDT-R2 (R1 = H, K, DK; R2 =



OH, L, LP, LPK) are claimed. Synthetic peptides, peptide fragments, and chem. modified peptides derived from a *Staphylococcus aureus* fibronectin-binding protein homol. unit (D3) were prepd., and the activity of the peptides (ability to compete with *S. aureus* cells for binding to 125I-labeled fibronectin or fragment) was detd. The fibronectin-binding region of D3 was reduced to a 14-residue core peptide essential for activity but alone not sufficient to inhibit binding; addn. of a tripeptide to the amino-terminus or carboxy-terminus of this core peptide resulted in a dramatic recovery of activity. The fibronectin-binding peptides of the invention can be used for vaccination, wound healing, blocking protein receptors, or for an ELISA.

SEQ 103

=> s hggniididfdsvp/sqep

0 HGGNIIDIDFDSVP/SQEP  
26675 SQL=14  
L32 0 HGGNIIDIDFDSVP/SQEP  
(HGGNIIDIDFDSVP/SQEP AND SQL=14)

=> s hggniididfdsvp/sqsp

L33 19 HGGNIIDIDFDSVP/SQSP

=> s l33 and sql<25

867298 SQL<25  
L35 1 L33 AND SQL<25

=> d sqide

L35 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS  
RN 155970-96-0 REGISTRY  
CN Glycine, L-lysyl-L-tyrosyl-L-.alpha.-glutamyl-L-histidylglycylglycyl-L-  
asparaginy-L-iso-leucyl-L-iso-leucyl-L-.alpha.-aspartyl-L-iso-leucyl-L-  
.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-seryl-L-valyl-L-  
prolyl-L-histidyl-L-iso-leucyl-L-histidyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*21\*\*\*

SEQ 1 KYEHGGNIID IDFDSVPHIH G

=====

HITS AT: 4-17

MF C106 H155 N29 O33

SR CA

LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus

=> s 155970-96-0/rn

1 155970-96-0  
0 155970-96-0D  
L38 1 155970-96-0/RN  
(155970-96-0 (NOTL) 155970-96-0D )

=> d ibib ab

L38 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 1994:452661 CAPLUS  
DOCUMENT NUMBER: 121:52661  
TITLE: Interaction of N-terminal fragments of fibronectin  
with synthetic and recombinant D motifs from its  
binding protein on Staphylococcus aureus studied using  
fluorescence anisotropy  
AUTHOR(S): Huff, Sheela; Matsuka, Yury V.; McGavin, Martin J.;

Ingham, Kenneth C.  
CORPORATE SOURCE: Holland Lab., Am. Red. Cross, Rockville, MD, 20855,  
USA  
SOURCE: J. Biol. Chem. (1994), 269(22), 15563-70  
CODEN: JBCHA3; ISSN: 0021-9258  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The N-terminal 29-kDa fragment of fibronectin (Fn29K) contains five type I "finger" modules. It binds to heparin, fibrin, and bacteria and is involved in fibronectin (Fn) matrix assembly. Binding to *Staphylococcus aureus* involves a cell wall-assocd. protein that contains .apprx.three repeats of a 38-residue D motif (Signas, C., Raucci, G., Jonsson, K., Lindgren, P.-E., Anantharamaiah, G. M., Hook, M., and Lindberg, M. (1989) Proc. Natl. Acad. Sci. U.S.A. 86, 699-703). Synthetic peptides representing D1, D2, and D3, when labeled with fluorescein isothiocyanate (FITC), exhibited increases in fluorescence anisotropy upon addn. of Fn29K but not other Fn fragments. The response could be reversed by titrn. with unlabeled peptides to yield inhibition consts. that agreed with the dissocn. consts. obtained by fitting the initial response. Values of Kd ranged between 2 and 12 .mu.M, with D3 having the highest affinity. Specificity of D3 for Fn29K was further illustrated by the fact that its C-terminal half (D3b, Lys801 to Lys821), when immobilized, selectively adsorbed Fn29K from a thermolysin digest of fibronectin. The binding site in Fn was further localized within Fn29K by analyzing smaller proteolytic or recombinant subfragments. Those contg. fingers, F3-5 and F4-5, were purified on D3b-Sepharose and bound FITC-D3b with Kd values of 4-6 .mu.m. Subfragments contg. pairs of fingers 1-2, 2-3, or single fingers 1, 4, or 5 were inactive. Whole D1-3, expressed in *Escherichia coli* and labeled with fluorescein, bound 1.9 mol/mol of Fn29K with Kd = 1.5 nM. F4-5 and F2-3 bound with resp. Kd values of 0.35 and 4.4 .mu.M. These and other results indicate that binding of the individual D region peptides is mediated through their C-terminal halves, primarily to fingers 4 and 5 of fibronectin. The possible basis of the much higher affinity of D1-3 is discussed.

SEQ 104

=> s svdfedt/sqep

0 SVDFEEDT/SQEP  
36664 SQL=8  
L39 0 SVDFEEDT/SQEP  
(SVDFEEDT/SQEP AND SQL=8)

=> s svdfedt/sqsp

L40 43 SVDFEEDT/SQSP

=> s l40 and sql<20

642596 SQL<20  
L41 10 L40 AND SQL<20

=> d sqide 1-10

L41 ANSWER 1 OF 10 REGISTRY COPYRIGHT 2001 ACS  
RN 264234-56-2 REGISTRY  
CN L-Leucine, L-phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-  
valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-  
glutamyl-L-.alpha.-aspartyl-L-threonyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*14\*\*\*

SEQ 1 FGGHNSVD FE EDTL  
=====

HITS AT: 6-13  
MF C68 H95 N17 O26  
SR CA  
LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L41 ANSWER 2 OF 10 REGISTRY COPYRIGHT 2001 ACS  
RN 142372-45-0 REGISTRY  
CN L-Proline, L-prolyl-L-seryl-L-tyrosyl-L-glutaminy-L-  
phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-valyl-L-  
.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-  
.alpha.-aspartyl-L-threonyl-L-leucyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*19\*\*\*

SEQ 1 PSYQFGGHNS VDFEEDTLP  
=====

HITS AT: 10-17  
MF C95 H131 N23 O34  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L41 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2001 ACS  
RN 142083-43-0 REGISTRY  
CN L-Threonine, L-.alpha.-aspartyl-L-lysyl-L-prolyl-L-seryl-L-tyrosyl-L-  
glutaminy-L-phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-

valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-  
glutamyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*19\*\*\*

SEQ 1 DKPSYQFGGH NSVDFEEDT

=====

HITS AT: 12-19

MF C94 H130 N24 O36

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L41 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2001 ACS

RN 142083-41-8 REGISTRY

CN L-Leucine, L-lysyl-L-prolyl-L-seryl-L-tyrosyl-L-glutaminy-L-  
phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-valyl-L-  
.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-  
.alpha.-aspartyl-L-threonyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL \*\*\*19\*\*\*

SEQ 1 KPSYQFGGHN SVDFEEDTL

=====

HITS AT: 11-18

MF C96 H136 N24 O34

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L41 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2001 ACS

RN 142083-40-7 REGISTRY

CN L-Threonine, L-lysyl-L-prolyl-L-seryl-L-tyrosyl-L-glutaminy-L-  
phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-valyl-L-  
.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-  
.alpha.-aspartyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL \*\*\*18\*\*\*

SEQ 1 KPSYQFGGHN SVDFEEDT

=====

HITS AT: 11-18

MF C90 H125 N23 O33

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L41 ANSWER 6 OF 10 REGISTRY COPYRIGHT 2001 ACS

RN 142083-38-3 REGISTRY

CN L-Leucine, L-prolyl-L-seryl-L-tyrosyl-L-glutaminy-L-  
phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-valyl-L-  
.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-  
.alpha.-aspartyl-L-threonyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL \*\*\*18\*\*\*

SEQ 1 PSYQFGGHNS VDFEEDTL

=====

HITS AT: 10-17

MF C90 H124 N22 O33

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L41 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2001 ACS

RN 142062-20-2 REGISTRY

CN L-Lysine, L-phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-threonyl-L-leucyl-L-prolyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL \*\*\*16\*\*\*

SEQ 1 FGGHNSVD FE EDTLPK

=====

HITS AT: 6-13

MF C79 H114 N20 O28

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L41 ANSWER 8 OF 10 REGISTRY COPYRIGHT 2001 ACS

RN 142062-19-9 REGISTRY

CN L-Threonine, L-glutaminyl-L-phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL \*\*\*14\*\*\*

SEQ 1 QFGGHNSVDF EEDT

=====

HITS AT: 7-14

MF C67 H92 N18 O27

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

3 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L41 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2001 ACS

RN 142062-18-8 REGISTRY

CN L-Lysine, L-glutaminyl-L-phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-threonyl-L-leucyl-L-prolyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL \*\*\*17\*\*\*

SEQ 1 QFGGHNSVDF EEDTLPK

=====

HITS AT: 7-14

MF C84 H122 N22 O30

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L41 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2001 ACS  
RN 142062-17-7 REGISTRY  
CN L-Threonine, L-prolyl-L-seryl-L-tyrosyl-L-glutaminyl-L-  
phenylalanylglycylglycyl-L-histidyl-L-asparaginy-L-seryl-L-valyl-L-  
.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-  
.alpha.-aspartyl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL \*\*\*17\*\*\*

SEQ 1 PSYQFGGHNS VDFEEDT  
= =====

HITS AT: 10-17  
MF C84 H113 N21 O32  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus uspatfull

=> s 264234-56-2/rn

L42 1 264234-56-2/RN

=> d ibib ab

L42 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 2000:146776 CAPLUS  
DOCUMENT NUMBER: 132:292413  
TITLE: Synthetic peptide immunogens elicit polyclonal and  
monoclonal antibodies specific for linear epitopes in  
the D motifs of Staphylococcus aureus  
fibronectin-binding protein, which are composed of  
amino acids that are essential for fibronectin binding  
AUTHOR(S): Huesca, Mario; Sun, Qing; Peralta, Robert; Shivji,  
Gulnar M.; Sauder, Daniel N.; McGavin, Martin J.  
CORPORATE SOURCE: Divisions of Microbiology, Laboratory Medicine and  
Pathobiology, Sunnybrook and Women's College Health  
Sciences Centre, North York, ON, M4N 3M5, Can.  
SOURCE: Infect. Immun. (2000), 68(3), 1156-1163  
CODEN: INFIBR; ISSN: 0019-9567  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB A fibronectin (Fn)-binding adhesin of Staphylococcus aureus contains three  
tandem 37- or 38-amino-acid motifs (D1, D2, and D3), which function to  
bind Fn. Plasma from patients with S. aureus infections contain  
antibodies that preferentially recognize ligand induced binding sites in  
the D motifs and do not inhibit Fn binding. To eliminate the influence of  
Fn binding on antibody development, the authors used synthetic peptide  
immunogens D121-34 and D320-33, which each contain a conserved pattern of  
amino acids that is essential for Fn binding but which cannot bind Fn  
without N- or C-terminal extensions. The D320-33 immunogen promoted the  
prodn. of polyclonal antibodies that were 10-fold more effective as  
inhibitors of Fn-binding to the D3 motif than antibodies obtained by

immunizing with an extended peptide D316-36, which exhibits functional Fn binding. The D320-33 immunogen also facilitated the prodn. of a monoclonal antibody, 9C3, which was highly specific for the epitope SVDFEED, and abolished Fn binding by the D3 motif. When mixed with polyclonal anti-D121-34 IgG, 70% inhibition of Fn binding to the three tandem D motifs was achieved compared to no more than 30% inhibition with either antibody prepn. alone. Therefore, by immunizing with short synthetic peptides that are unable to bind Fn, the authors have effectively stimulated the prodn. of antibodies specific for epitopes comprised of amino acids that are essential for Fn binding. Although these epitopes occur within a conserved pattern of amino acids that is required for Fn binding, the antibodies recognized specific linear epitope sequences and not a conserved structure common to all repeated motifs.

REFERENCE COUNT: 40

REFERENCE(S): (3) Balaban, N; Science 1998, V280, P438 CAPLUS  
 (4) Brennan, F; Vaccine 1999, V17, P1846 CAPLUS  
 (5) Casolini, F; Infect Immun 1998, V66, P5433 CAPLUS  
 (6) Fattom, A; Ann Med 1996, V28, P43 CAPLUS  
 (7) Fattom, A; Infect Immun 1996, V64, P1659 CAPLUS  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s (142372-45-0 or 142083-43-0 or 142083-41-8 or 142083-40-7 or 142083-38-3)/rn

L43 2 (142372-45-0 OR 142083-43-0 OR 142083-41-8 OR 142083-40-7 OR 142083-38-3)/RN

=> d ibib ab hit 1 2

L43 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:444088 CAPLUS

DOCUMENT NUMBER: 117:44088

TITLE: Chemically modified fibronectin-binding peptides and fragments

INVENTOR(S): Hoeoek, Magnus; McGavin, Martin; Raucci, Guiseppe

PATENT ASSIGNEE(S): Alfa-Laval Agri International AB, Swed.

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9202555	A1	19920220	WO 1991-SE534	19910809
W: AU, CA, FI, HU, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2067233	AA	19920211	CA 1991-2067233	19910809
AU 9184118	A1	19920302	AU 1991-84118	19910809
AU 632001	B2	19921210		
EP 504335	A1	19920923	EP 1991-914903	19910809
EP 504335	B1	19971210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 61035	A2	19921130	HU 1992-1211	19910809
HU 219261	B	20010328		
JP 05502046	T2	19930415	JP 1991-514015	19910809
AT 161018	E	19971215	AT 1991-914903	19910809
ES 2112862	T3	19980416	ES 1991-914903	19910809
FI 9201582	A	19920409	FI 1992-1582	19920409
NO 9201407	A	19920605	NO 1992-1407	19920409



US 5440014 A 19950808 US 1994-234622 19940428  
PRIORITY APPLN. INFO.: SE 1990-2617 A 19900810  
WO 1991-SE534 A 19910809  
US 1992-846995 B1 19920608  
US 1993-55783 B1 19930503

OTHER SOURCE(S): MARPAT 117:44088

AB Fibronectin-binding peptides R1-PSYQFGGHNSVDFEEDT-R2 (R1 = H, K, DK; R2 = OH, L, LP, LPK) are claimed. Synthetic peptides, peptide fragments, and chem. modified peptides derived from a Staphylococcus aureus fibronectin-binding protein homol. unit (D3) were prepd., and the activity of the peptides (ability to compete with S. aureus cells for binding to 125I-labeled fibronectin or fragment) was detd. The fibronectin-binding region of D3 was reduced to a 14-residue core peptide essential for activity but alone not sufficient to inhibit binding; addn. of a tripeptide to the amino-terminus or carboxy-terminus of this core peptide resulted in a dramatic recovery of activity. The fibronectin-binding peptides of the invention can be used for vaccination, wound healing, blocking protein receptors, or for an ELISA.

IT \*\*\*142083-38-3\*\*\* 142083-39-4 \*\*\*142083-40-7\*\*\*  
\*\*\*142083-41-8\*\*\* 142083-42-9 \*\*\*142083-43-0\*\*\* 142083-44-1  
142083-45-2 142083-46-3 \*\*\*142372-45-0\*\*\*

RL: ANST (Analytical study)  
(fibronectin binding peptide amino acid sequence)

L43 ANSWER 2 OF 2 USPATFULL

ACCESSION NUMBER: 95:71464 USPATFULL

TITLE: Fibronectin binding peptide

INVENTOR(S): Hook, Magnus, 129 Stevens Hill Cir., Birmingham, AL,  
United States 35244  
McGavin, Martin, 1717 Beacon Crest Cir., Birmingham,  
AL, United States 35209  
Raucci, Guiseppe, Via Tito Speri 10, I-00040 Pomezia,  
Rome, Italy

NUMBER KIND DATE

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PATENT INFORMATION: US 5440014 19950808  
APPLICATION INFO.: US 1994-234622 19940428 (8)  
RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-55783, filed on 3 May  
1993, now abandoned which is a continuation of Ser. No.  
US 1992-846995, filed on 8 Jun 1992, now abandoned

NUMBER DATE

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PRIORITY INFORMATION: SE 1990-2617 19900810  
DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Warden, Jill  
ASSISTANT EXAMINER: Marshall, S. G.  
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis  
NUMBER OF CLAIMS: 1  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)  
LINE COUNT: 679

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A fibronectin binding peptide having the structure R'-PSYQFGGHNS  
VDFEEDT-R.sup.2 wherein R' is hydrogen, K or DK, and R.sup.2 is hydroxy,  
L, LP or LPK is disclosed. The fibronectin binding proteins of the  
present invention may be used, for example, for vaccination of ruminants  
against mastitis caused by Staphylococcal infections, for the treatment  
of wounds, e.g., for blocking protein receptors or for immunization  
(vaccination) against infection by bacterial strains, and for diagnosis

of bacterial infections caused by Staphylococci strains.

IT \*\*\*142083-38-3\*\*\* 142083-39-4 \*\*\*142083-40-7\*\*\*  
\*\*\*142083-41-8\*\*\* 142083-42-9 \*\*\*142083-43-0\*\*\* 142083-44-1  
142083-45-2 142083-46-3 \*\*\*142372-45-0\*\*\*  
(fibronectin binding peptide amino acid sequence)

=> s (142062-20-2 or 142062-19-9 or 142062-18-8 or 142062-17-7)/rn

L44 4 (142062-20-2 OR 142062-19-9 OR 142062-18-8 OR 142062-17-7)/RN

=> d ibib ab hit 1-4

L44 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:146776 CAPLUS

DOCUMENT NUMBER: 132:292413

TITLE: Synthetic peptide immunogens elicit polyclonal and  
monoclonal antibodies specific for linear epitopes in  
the D motifs of Staphylococcus aureus  
fibronectin-binding protein, which are composed of  
amino acids that are essential for fibronectin binding

AUTHOR(S): Huesca, Mario; Sun, Qing; Peralta, Robert; Shivji,  
Gulnar M.; Sauder, Daniel N.; McGavin, Martin J.

CORPORATE SOURCE: Divisions of Microbiology, Laboratory Medicine and  
Pathobiology, Sunnybrook and Women's College Health  
Sciences Centre, North York, ON, M4N 3M5, Can.

SOURCE: Infect. Immun. (2000), 68(3), 1156-1163

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A fibronectin (Fn)-binding adhesin of Staphylococcus aureus contains three  
tandem 37- or 38-amino-acid motifs (D1, D2, and D3), which function to  
bind Fn. Plasma from patients with S. aureus infections contain  
antibodies that preferentially recognize ligand induced binding sites in  
the D motifs and do not inhibit Fn binding. To eliminate the influence of  
Fn binding on antibody development, the authors used synthetic peptide  
immunogens D121-34 and D320-33, which each contain a conserved pattern of  
amino acids that is essential for Fn binding but which cannot bind Fn  
without N- or C-terminal extensions. The D320-33 immunogen promoted the  
prodn. of polyclonal antibodies that were 10-fold more effective as  
inhibitors of Fn-binding to the D3 motif than antibodies obtained by  
immunizing with an extended peptide D316-36, which exhibits functional Fn  
binding. The D320-33 immunogen also facilitated the prodn. of a  
monoclonal antibody, 9C3, which was highly specific for the epitope  
SVDFEED, and abolished Fn binding by the D3 motif. When mixed with  
polyclonal anti-D121-34 IgG, 70% inhibition of Fn binding to the three  
tandem D motifs was achieved compared to no more than 30% inhibition with  
either antibody prepn. alone. Therefore, by immunizing with short  
synthetic peptides that are unable to bind Fn, the authors have  
effectively stimulated the prodn. of antibodies specific for epitopes  
comprised of amino acids that are essential for Fn binding. Although  
these epitopes occur within a conserved pattern of amino acids that is  
required for Fn binding, the antibodies recognized specific linear epitope  
sequences and not a conserved structure common to all repeated motifs.

REFERENCE COUNT: 40

REFERENCE(S): (3) Balaban, N; Science 1998, V280, P438 CAPLUS

(4) Brennan, F; Vaccine 1999, V17, P1846 CAPLUS

(5) Casolini, F; Infect Immun 1998, V66, P5433 CAPLUS

(6) Fattom, A; Ann Med 1996, V28, P43 CAPLUS

(7) Fattom, A; Infect Immun 1996, V64, P1659 CAPLUS

## ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 142062-16-6 \*\*\*142062-19-9\*\*\* 264234-56-2

RL: BAC (Biological activity or effector, except adverse); PRP

(Properties); BIOL (Biological study)

(peptide immunogens elicit polyclonal and monoclonal antibodies that inhibit fibronectin-binding protein of Staphylococcus aureus)

L44 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:509122 CAPLUS

DOCUMENT NUMBER: 129:148069

TITLE: Fibronectin binding protein compositions, antibodies  
thereto, and methods of useINVENTOR(S): Hook, Magnus; Patti, Joseph M.; House-Pompeo, Karen  
L.; Speziale, Petro; Joh, Danny; McGavin, Martin J.

PATENT ASSIGNEE(S): The Texas A &amp; M University System, USA

SOURCE: PCT Int. Appl., 201 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO 9831389 A2 19980723 WO 1998-US1222 19980121

WO 9831389 A3 19990121

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,  
DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,  
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,  
FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,  
GA, GN, ML, MR, NE, SN, TD, TG

AU 9866479 A1 19980807 AU 1998-66479 19980121

EP 971740 A2 20000119 EP 1998-908439 19980121

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1997-36139 19970121

WO 1998-US1222 19980121

AB Disclosed are antibodies that block the binding of fibronectin protein to fibronectin. Also disclosed are site specifically-mutated and truncated peptide epitopes derived from the fnbA and fnbB genes of Staphylococcus aureus, the fnbA and fnbB genes of Streptococcus dysgalactiae, and the sfb gene of Streptococcus pyogenes, and nucleic acid segments encoding these peptides and epitopes. The anti-(fibronectin binding site) antibodies, peptides and epitopes that give rise to antibodies that block the binding of fibronectin binding proteins to fibronectin, and DNA segments encoding these proteins and are of use in various screening, diagnostic and therapeutic applications including active and passive immunization and methods for the prevention of streptococcal and staphylococcal colonization in animals or humans. These DNA segments and the peptides derived therefrom are proposed to be of use directly in the prepn. of vaccines and also for use as carrier proteins in vaccine formulations.

IT \*\*\*142062-19-9P\*\*\* 187102-34-7P

RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(microbial fibronectin binding protein epitopes and their antibodies for diagnosing and preventing infection)

L44 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:444088 CAPLUS  
 DOCUMENT NUMBER: 117:44088  
 TITLE: Chemically modified fibronectin-binding peptides and fragments  
 INVENTOR(S): Hoeoek, Magnus; McGavin, Martin; Raucchi, Guiseppe  
 PATENT ASSIGNEE(S): Alfa-Laval Agri International AB, Swed.  
 SOURCE: PCT Int. Appl., 32 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9202555	A1	19920220	WO 1991-SE534	19910809
W: AU, CA, FI, HU, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2067233	AA	19920211	CA 1991-2067233	19910809
AU 9184118	A1	19920302	AU 1991-84118	19910809
AU 632001	B2	19921210		
EP 504335	A1	19920923	EP 1991-914903	19910809
EP 504335	B1	19971210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 61035	A2	19921130	HU 1992-1211	19910809
HU 219261	B	20010328		
JP 05502046	T2	19930415	JP 1991-514015	19910809
AT 161018	E	19971215	AT 1991-914903	19910809
ES 2112862	T3	19980416	ES 1991-914903	19910809
FI 9201582	A	19920409	FI 1992-1582	19920409
NO 9201407	A	19920605	NO 1992-1407	19920409
US 5440014	A	19950808	US 1994-234622	19940428
PRIORITY APPLN. INFO.: SE 1990-2617 A 19900810				
WO 1991-SE534 A 19910809				
US 1992-846995 B1 19920608				
US 1993-55783 B1 19930503				

OTHER SOURCE(S): MARPAT 117:44088

AB Fibronectin-binding peptides R1-PSYQFGGHNSVDFEEDT-R2 (R1 = H, K, DK; R2 = OH, L, LP, LPK) are claimed. Synthetic peptides, peptide fragments, and chem. modified peptides derived from a Staphylococcus aureus fibronectin-binding protein homol. unit (D3) were prepd., and the activity of the peptides (ability to compete with S. aureus cells for binding to 125I-labeled fibronectin or fragment) was detd. The fibronectin-binding region of D3 was reduced to a 14-residue core peptide essential for activity but alone not sufficient to inhibit binding; addn. of a tripeptide to the amino-terminus or carboxy-terminus of this core peptide resulted in a dramatic recovery of activity. The fibronectin-binding peptides of the invention can be used for vaccination, wound healing, blocking protein receptors, or for an ELISA.

IT 142062-16-6 \*\*\*142062-17-7\*\*\*

RL: BAC (Biological activity or effector, except adverse); BIOL  
 (Biological study)  
 (amino acid sequence and fibronectin binding activity of)

IT 56-82-6D, DL-Glyceraldehyde, fibronectin binding protein synthetic D3 fragment reaction products 141-43-5D, fibronectin binding protein synthetic D3 fragment reaction products 509-14-8D, Tetranitromethane, fibronectin binding protein synthetic D3 fragment reaction products 616-34-2D, Glycine methyl ester, fibronectin binding protein synthetic D3 fragment reaction products \*\*\*142062-18-8\*\*\* \*\*\*142062-19-9\*\*\*  
 \*\*\*142062-20-2\*\*\*

RL: BAC (Biological activity or effector, except adverse); BIOL  
 (Biological study)

(fibronectin binding activity of)

L44 ANSWER 4 OF 4 USPATFULL

ACCESSION NUMBER: 95:71464 USPATFULL

TITLE: Fibronectin binding peptide

INVENTOR(S): Hook, Magnus, 129 Stevens Hill Cir., Birmingham, AL,  
United States 35244  
McGavin, Martin, 1717 Beacon Crest Cir., Birmingham,  
AL, United States 35209  
Raucci, Guiseppe, Via Tito Speri 10, I-00040 Pomezia,  
Rome, Italy

NUMBER KIND DATE

PATENT INFORMATION: US 5440014 19950808

APPLICATION INFO.: US 1994-234622 19940428 (8)

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NUMBER DATE

PRIORITY INFORMATION: SE 1990-2617 19900810

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Warden, Jill

ASSISTANT EXAMINER: Marshall, S. G.

LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis

NUMBER OF CLAIMS: 1

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)

LINE COUNT: 679

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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VDFEEDT-R.sup.2 wherein R' is hydrogen, K or DK, and R.sup.2 is hydroxy,  
L, LP or LPK is disclosed. The fibronectin binding proteins of the  
present invention may be used, for example, for vaccination of ruminants  
against mastitis caused by Staphylococcal infections, for the treatment  
of wounds, e.g., for blocking protein receptors or for immunization  
(vaccination) against infection by bacterial strains, and for diagnosis  
of bacterial infections caused by Staphylococci strains.

IT 142062-16-6 \*\*\*142062-17-7\*\*\*

(amino acid sequence and fibronectin binding activity of)

IT 56-82-6D, DL-Glyceraldehyde, fibronectin binding protein synthetic D3  
fragment reaction products 141-43-5D, fibronectin binding protein  
synthetic D3 fragment reaction products 509-14-8D, Tetranitromethane,  
fibronectin binding protein synthetic D3 fragment reaction products  
616-34-2D, Glycine methyl ester, fibronectin binding protein synthetic D3  
fragment reaction products \*\*\*142062-18-8\*\*\* \*\*\*142062-19-9\*\*\*  
\*\*\*142062-20-2\*\*\*

(fibronectin binding activity of)

SEQ 6

=> s qnsgnqsfeedteedkpkyeqpgnivdidfdsvpqihg/sqep

0 QNSGNQSFEEDTEEDKPKYEQPGNIVDIDFDSVPQIHG/SQEP

23669 SQL=38

L11 0 QNSGNQSFEEDTEEDKPKYEQPGNIVDIDFDSVPQIHG/SQEP

(QNSGNQSFEEDTEEDKPKYEQPGNIVDIDFDSVPQIHG/SQEP AND SQL=38)

=> s qnsgnqsfeedteedkpkyeqpgnivdidfdsvpqihg/sqsp

L12 0 QNSGNQSFEEDTEEDKPKYEQPGNIVDIDFDSVPQIHG/SQSP

*Free of art*

SEQ 8

=> s qnkgnsfeedtekdkpkYehpgniididfdsvphiHg/sqep

0 QNKGNSFEEDTEKDKPKYEHpgniididfdsvphiHg/SQEP

23669 SQL=38

L15 0 QNKGNSFEEDTEKDKPKYEHpgniididfdsvphiHg/SQEP

(QNKGNSFEEDTEKDKPKYEHpgniididfdsvphiHg/SQEP AND SQL=38)

=> s qnkgnsfeedtekdkpkYehpgniididfdsvphiHg/sqsp

L16 0 QNKGNSFEEDTEKDKPKYEHpgniididfdsvphiHg/SQSP

SEQ ID NO:13

=> s kpsyqfpghnsvdfeedtlpkv/sqep

0 KPSYQFPGHNSVDFEEDTLPKV/SQEP

28563 SQL=22

L20 0 KPSYQFPGHNSVDFEEDTLPKV/SQEP

(KPSYQFPGHNSVDFEEDTLPKV/SQEP AND SQL=22)

=> s kpsyqfpghnsvdfeedtlpkv/sqsp

L21 0 KPSYQFPGHNSVDFEEDTLPKV/SQSP



SEQ ID NO:17

=> s kpspqfghnsvdfeedtlpkv/sqep

0 KPSPQFGGHNSVDFEEDTLPKV/SQEP

28563 SQL=22

L22 0 KPSPQFGGHNSVDFEEDTLPKV/SQEP

(KPSPQFGGHNSVDFEEDTLPKV/SQEP AND SQL=22)

=> s kpspqfghnsvdfeedtlpkv/sqsp

L23 0 KPSPQFGGHNSVDFEEDTLPKV/SQSP

SEQ ID NO:18

=> s kpsypfghnsvdfeedtlpk/sqep

0 KPSYPFGGHNSVDFEEDTLPK/SQEP

50328 SQL=21

L24 0 KPSYPFGGHNSVDFEEDTLPK/SQEP

(KPSYPFGGHNSVDFEEDTLPK/SQEP AND SQL=21)

=> s kpsypfghnsvdfeedtlpk/sqsp

L25 0 KPSYPFGGHNSVDFEEDTLPK/SQSP

SEQ ID NO:19

=> s kpsyqpgghnsvdfeedtlpk/sqep

0 KPSYQPGGHNSVDFEEDTLPK/SQEP

50328 SQL=21

L26 0 KPSYQPGGHNSVDFEEDTLPK/SQEP

(KPSYQPGGHNSVDFEEDTLPK/SQEP AND SQL=21)

=> s kpsyqpgghnsvdfeedtlpk/sqsp

L27 0 KPSYQPGGHNSVDFEEDTLPK/SQSP

SEQ ID NO:20

=> s kpsyqfgphnsvdfeedtlpk/sqep

0 KPSYQFGPHNSVDFEEDTLPK/SQEP

50328 SQL=21

L28 0 KPSYQFGPHNSVDFEEDTLPK/SQEP

(KPSYQFGPHNSVDFEEDTLPK/SQEP AND SQL=21)

=> s kpsyqfgphnsvdfeedtlpk/sqsp

L29 0 KPSYQFGPHNSVDFEEDTLPK/SQSP

SEQ 54

=> s advveyeedtnpgpgqvtttesnlvefdeest/sqep

0 ADVVEYEEDTNPGPGQVTTESNLVEFDEEST/SQEP

20887 SQL=31

L1 0 ADVVEYEEDTNPGPGQVTTESNLVEFDEEST/SQEP

(ADVVEYEEDTNPGPGQVTTESNLVEFDEEST/SQEP AND SQL=31)

=> s advveyeedtnpgpgqvtttesnlvefdeest/sqsp

L2 0 ADVVEYEEDTNPGPGQVTTESNLVEFDEEST/SQSP

SEQ 55

=> s advveyppdtnpppgqvtttesnlvefdeest/sqep

0 ADVVEYPPDTNPPPGQVTTESNLVEFDEEST/SQEP

20887 SQL=31

L1 0 ADVVEYPPDTNPPPGQVTTESNLVEFDEEST/SQEP  
(ADVVEYPPDTNPPPGQVTTESNLVEFDEEST/SQEP AND SQL=31)

=> s advveyppdtnpppgqvtttesnlvefdeest/sqsp

L2 0 ADVVEYPPDTNPPPGQVTTESNLVEFDEEST/SQSP

SEQ 56

=> s qnsgnqsfeedteedkpkyeqggnivdidfsdsvpqihg/sqep

0 QNSGNQSFEEDTEEDKPKYEQGGNIVDIDFSDSVQIHG/SQEP

8634 SQL=39

L3 0 QNSGNQSFEEDTEEDKPKYEQGGNIVDIDFSDSVQIHG/SQEP

(QNSGNQSFEEDTEEDKPKYEQGGNIVDIDFSDSVQIHG/SQEP AND SQL=39)

=> s qnsgnqsfeedteedkpkyeqggnivdidfsdsvpqihg/sqsp

L4 0 QNSGNQSFEEDTEEDKPKYEQGGNIVDIDFSDSVQIHG/SQSP

SEQ 57

=> s qnsgnqsfeedteedkpkyeqpgnivdidfsdsvpqihg/sqep

0 QNSGNQSFEEDTEEDKPKYEQPGNIVDIDFSDSVQIHG/SQEP

8634 SQL=39

L5 0 QNSGNQSFEEDTEEDKPKYEQPGNIVDIDFSDSVQIHG/SQEP

(QNSGNQSFEEDTEEDKPKYEQPGNIVDIDFSDSVQIHG/SQEP AND SQL=39)

=> s qnsgnqsfeedteedkpkyeqpgnivdidfsdsvpqihg/sqsp

L6 0 QNSGNQSFEEDTEEDKPKYEQPGNIVDIDFSDSVQIHG/SQSP



SEQ 59

=> s qnkgnsfeedtekdkyehpgniididfdsvphihg/sqep

0 QNKGNSFEEDTEKDKYEHPGNIIDIDFDSVPHIHG/SQEP

19158 SQL=36

L9 0 QNKGNSFEEDTEKDKYEHPGNIIDIDFDSVPHIHG/SQEP

(QNKGNSFEEDTEKDKYEHPGNIIDIDFDSVPHIHG/SQEP AND SQL=36)

=> s qnkgnsfeedtekdkyehpgniididfdsvphihg/sqsp

L10 0 QNKGNSFEEDTEKDKYEHPGNIIDIDFDSVPHIHG/SQSP